Selected Prescription Drug Usage In Utah, 2003

Utah Health Data Committee
Health Plan Pharmacy Data Oversight Committee

Office of Health Care Statistics
Center for Health Data
Utah Department of Health

July 2005

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http://health.utah.gov/hda/pharmacy/RxIndicators.pdf

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"The purpose of the [Utah health data] committee is to direct a statewide effort to collect, analyze, and distribute health care data to facilitate the promotion and accessibility of quality and cost-effective health care and also to facilitate interaction among those with concern for health care issues."

Utah Code Title 26 Chapter 33a, Utah Health Data Authority Act 26-33a-104(1)

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Utah Pharmacy Data Plan, Version 1

http://health.utah.gov/hda/UtahPharmacyDataPlan.pdf

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SECTION I

Introduction

Health care purchasers, providers, payers, public health programs, federal and state health officials have devoted considerable attention to medication safety and the rising cost of prescription drugs in the nation and states. Many policy and research questions relating to prescription drugs and non-acute morbidity status of a population cannot be answered without a pharmacy database.

Utah Health Data Committee (HDC), a Utah Governor appointed statutory committee in Utah Department of Health (UDOH), launched a new statewide initiative to collect and report pharmacy data. The purpose of this initiative is to create a statewide pharmacy database and use the data for public health surveillance of outpatient morbidity, improvements in appropriate uses of prescription drugs, medication safety, and other prescription drug-related research projects.

The Utah Pharmacy Data Advisory Committee (UPDAC) created by the HDC, has guided the Office of Health Care Statistics (OHCS) in the development of the Utah Pharmacy Data Plan Version 1. The Utah Pharmacy Data Plan issued in April 2004 documented the feasibility study and available pharmacy data sources. The UPDAC selected ten pharmacy indicators for public reporting. The Plan also addressed implementation issues, such as confidentiality, database standards, health plan participation agreement, database management, and coordination of financial resources.

The HDC established the Health Plan Pharmacy Data Oversight Committee (HPPDOC) to steer the implementation of the Utah Pharmacy Data Plan, Phase I. The Method Advisory Group leads in the technical development of the report. This report is based upon prescription claims data from voluntarily participating health plans in Utah. The data in the indicator tables were verified by each participating health plans. Committee members, sponsoring public health programs, and interested parties reviewed two draft versions of the report. This report is a product of community-wide collaboration.

The HPPDOC strongly encourages public health programs, health plans, quality improvement organizations, and health service researchers to use these statewide pharmacy data for intervention. The committee hopes that this report can be used for community-based patient and provider education; intervention needs assessment, and evaluation of quality improvement projects. Improvement of the health of Utahns is the ultimate goal of the Utah Health Data Committee's Pharmacy Data Initiative.

SECTION II

Executive Summary

This report is based on 2003 calendar year pharmacy claims data voluntarily submitted by Altius Health Plans, IHC Health Plans, Public Employees Health Plans, and Utah Division of Health Care Finance/Medicaid Program. Roughly 47% of the insured population in Utah is represented in this report. Nearly one million people (a total of 861275 member-years) from the above plans received one or more prescriptions from one of the ten pharmacy indicators (some people with dual plan coverage will be counted more than once). In addition to claims data, participating plans also submitted aggregate membership data to be used in prevalence calculations.

There are ten measures in the report, including seven related to chronic disease and three focused on utilization. At the core of each of these measures are the data tables with detailed measures based on the pharmacy claims data submitted by the participating health plans. While the tables will vary depending on the indicator, the two main types of measures in data tables are:

Prevalence: How many patients receive medications in a certain class?

Compliance: Once patients start treatment for chronic disease, what proportion of the time over the rest of the year do they receive their medications?

The ten indicators are:

- Hypertension
- Diabetes
- Hypercholesterolemia
- Asthma
- Adolescent Depression
- Depression, OCD and Anxiety Disorders in Pregnancy
- Use of Antipsychotics
- Use of Antibiotics
- Pain Management
- Use of Generics

Prevalence tables, in addition to allowing comparisons among different patient groups by age, gender and patient location, also present information on which drug classes are prescribed most often for different diseases.

Compliance tables address how well patients that should be receiving medications routinely are doing. While poorer performance here can be the result of a number of causes, these tables are aimed at pinpointing specific targets for intervention.

While each of the ten pharmacy indicators has findings of note, three significant key findings are:

Hypertension:

1) Of patients in the hypertension indicator, just under half received a diuretic.

While there is compelling evidence regarding the effectiveness of diuretics in treating hypertension, Utah is in line with national data showing underutilization of these

drugs. As many diuretics are also inexpensive, this represents an opportunity to improve treatment of hypertension in a cost effective manner.

Asthma:

2) Forty percent of patients in the asthma indicator receive only rescue/quick-relief medications.

One of the cornerstones of asthma treatment is long-term management; that is, treatment with medications for long-term maintenance/control of asthma in order to limit disease progression and lessen the likelihood of asthma attacks. Ideally, routine use of long-term control medications for asthma will decrease reliance on quick-relief medications. Many asthma patients in Utah are relying on only quick-relief medications for treatment of their disease.

3) For those asthma patients receiving long-term control medications, compliance is relatively low.

For both measures of compliance used in this report (medication possession ratio and persistence), compliance figures for asthma long-term control medications compare poorly to compliance figures for other chronic diseases in this report.

As asthma attacks can often lead to visits to the emergency room, both of these findings represent areas where education provides an opportunity to improve quality of asthma care and at the same time decrease burden on the healthcare system.

Some key findings from the other eight indicators include the following:

Diabetes: Over one-third of patients (37%) receive combination therapy (more than one drug class).

Hypercholesterolemia: The majority of patients are treated with only one drug class. Only 9% of patients are on combination therapy.

Adolescent depression: Rate of antidepressant use among those aged 10-17 is roughly 40% that of adults 18 and over.

Depression, OCD and Anxiety Disorders during Pregnancy: Selective Serotonin Reuptake Inhibitors (SSRIs) -- including fluoxetine (Prozac), paroxetine (Paxil), and

venlafaxine (Effexor) – were the most commonly prescribed class, with 77% of patients receiving a drug from this class.

Antipsychotics: The rate of antipsychotic use is roughly twice as high among urban patients as rural patients.

Antibiotics: Antibiotic use is highest in children aged 0-4 and adults over 85.

Pain: Use of pain medications tends to increase with age. In addition, women are roughly 50% more likely than men to receive pain medications.

Generics: People aged 5-17 were less likely to receive generics than other age groups.

The key findings for each of the pharmacy indicators present opportunities for learning about important areas of chronic disease such as disease prevalence, treatment, utilization of different drug classes, and patient compliance. In addition, as the indicator data tables break out information into age group, gender, and patient location (urban/rural), users with more specific interests can compare patterns of use among different population groups.

Looking forward, this report can serve as a baseline for future reports and presents a starting point from which trend data can be examined. It is hoped that this report will provide answers to some questions while spurring new avenues of inquiry.

The Utah pharmacy data initiative was created for the purpose of using pharmacy data for statewide monitoring and better understanding of prescription drug usage. Utah Health Data Committee will work with participating health plans and public health programs to reach the initiative's ultimate goal - improvement of the health of Utahns.

SECTION III

Data, Methodology and Limitations

I. Data source, standards

Pharmacy claims data for calendar year 2003 were submitted by Altius Health Plans, IHC Health Plans, Public Employees Health Plans, and Utah Division of Health Care Finance/Medicaid Program. For Altius Health Plans and IHC Health Plans data for commercial HMO members were submitted. Public Employees Health Plans and Utah Division of Health Care Finance/Medicaid Program submitted data for all members.

Aggregate plan membership data were also submitted by the above organizations. This was used in prevalence calculations detailing indicators by age group, gender, and location (urban/rural).

II. Measures

Seven of the indicators in this document – **hypertension, diabetes, hypercholesterolemia, asthma, adolescent depression, depression and other disorders during pregnancy,** and **use of antipsychotics** – will have the same three core tables.

These are:

1. **Prevalence**: Number of patients receiving particular drug therapy(ies). This is expressed both in counts of plan members receiving one or more drugs from a particular class and as a rate of plan members per 1000 member years.
2. **Medication possession ratio (MPR)**: Proportion of time a patient receives a particular drug
3. **Persistence:** Describes length of time (in days) a patient goes without a drug

Asthma will have one additional table focusing on use of rescue/quick-relief medications.

Two indicators – **use of antibiotics** and **pain medications** – will have only the prevalence table, as MPR and persistence are not appropriate for these indicators.

Finally, **use of generics** – the tenth indicator – will have two tables focusing on comparative use of generics vs. brand name prescribing for a selected list of medications.

For compliance it was felt that **Medication Possession Ratio (MPR)** would be the most useful metric. As plan entrance and exit can not be definitively determined from the data source, making the best possible proxy assumptions were discussed by the Utah Pharmacy Project Method Advisory Group. The group decided that, given the known limitations, the most accurate method of determining MPR would be to take prescription start date for a therapeutic class as beginning of MPR measurement, with end date of prescription therapy as end date for MPR measurement. For example:

	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Drug supplied to patient **A**:				**YES**	**YES**	**YES**			**YES**			
Medication possession ratio = 0.66	(APR + MAY + JUN + SEP)/(APR + MAY + JUN + JUL + AUG + SEP)											

Using persistence in conjunction with the MPR will allow to better profile trends of drug use. For example, for both patients below the MPR is roughly one-half. However, the lapses where the patient is without the drug are smaller for patient C. The smaller persistence number illustrates this fact.

	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Drug supplied to patient **B**:	**YES**	**YES**	**YES**							**YES**	**YES**	**YES**
Medication possession ratio = 0.5	(JAN + FEB + MAR + OCT + NOV + DEC)/(365 DAYS)											
Persistence = 183 days												

	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Drug supplied to patient **C**:	**YES**		**YES**		**YES**		**YES**		**YES**			**YES**
Medication possession ratio = 0.5	(JAN + MAR + MAY + JUL + SEP + DEC)/(365 DAYS)											
Persistence = 36 days (mean) 30 days (median)												

Definite plan entry and exit dates for participants are not known in the available data. As such, decision rules used to calculate medication possession ratio and persistence will likely yield:

- a higher (more favorable) MPR value than is the case

- a lower (more favorable) persistence value than is the case

Drug classes in this report were generated by classifying individual drugs (all manufacturers and doses) and grouping them into classes. This resulted in the following unique capabilities:

1) Classification of combination drugs

Drugs consisting of two or more agents, such as antihypertensive drugs that contain ***both*** ACE Inhibitors and diuretics, are dealt with by existing classification schemes in a number of ways. For example, for a combination medicine containing drugs from classes "A" and "B", it could be classified:

- As a class "A" medication
- As a class "B" medication
- In a specific class just for class A/B combination medicines
- In a more general combination class
- Or, finally, in a catch all miscellaneous class

Classification of combination drugs, even within existing systems, tended to be imprecise and inconsistent.

As one of the goals of this project was to ascertain as best as possible treatment patterns, all combination drugs in this report were accounted for in each appropriate therapeutic class.

2) Classification of drugs within a class

Some indicators rely on breaking out drugs within a drug class. For example, the asthma indicator looks at use of quick-relief beta agonists. As beta agonists also include drugs used for long-term control, splitting drugs within the beta-agonist class was performed for this report.

III. Limitations of data

1) The pharmacy claims analyzed in this report are from calendar year 2003. New drugs/drug classes introduced since then will not be included. The fact this is calendar year 2003 data should also be kept in mind when comparing practices/patterns in this report to findings in research studies published since 2003.

2) Diagnosis data are not present in the data source. One of the rationales behind indicator creation was selection of diseases for which drug treatment is relatively specific. While this is less of an issue with some diseases where treatment is rather specific (hypercholesterolemia, diabetes), it does play a role in some indicators (patients with chronic obstructive pulmonary disease (COPD) being included in the asthma indicator, congestive heart failure (CHF) patients being included in the hypertension indicator).

3) These data represent outpatient claims only. This does not allow for examination of drug trends in settings such as the acute care hospital. In addition, drug classes consisting exclusively/predominantly of drugs administered intravenously (rather than orally) were excluded.

4) Definite plan entry and exit dates for plan participants are not known. When assumptions had to be made, they were conservative ones that resulted in higher (more favorable) MPR and lower (more favorable) persistence.

5) While patients could be tracked longitudinally within a health plan, patients that had dual plan coverage could not be linked across plans. As a result, deduplication of these patients in the Utah statewide pharmacy database was not possible (meaning that in some cases patients will be counted more than once).

6) For prevalence calculations, a rate of patients per 1000 member years was calculated. As this is not a true ratio, this figure can be more or less than 1000 patients per 1000 member years. There are existing studies using more refined methodology that have attempted to determine disease prevalence for chronic diseases like diabetes and hypertension. Limitations such as lack of diagnosis data and inability to deduplicate (in 2) and 5), above) make precise prevalence determinations difficult. **The most appropriate use of prevalence calculations from this report is for comparative purposes – for example, examining differences between age groups or gender.**

7) Participation in this project was voluntary. As such, Utah Division of Health Care Finance/Medicaid Program is overrepresented in both the young and old age groups in this sample as not all health plans are represented.

SECTION IV

Pharmacy Indicators

Indicator 1 - Hypertension

Hypertension - Introduction

Hypertension, or high blood pressure, is a common disease affecting roughly 65 million people in the U.S. It tends to be more common with increasing age and frequently goes untreated as it may not cause acute symptoms. Long-term consequences of hypertension can include stroke, heart failure, and kidney disease. Hypertension is diagnosed after blood pressure measurements over time are determined to be high.

This indicator focuses on use of four major classes of drugs used to treat hypertension:

- Diuretics
- Beta-blockers
- Calcium channel blockers
- ACE (angiotensin converting enzyme) inhibitors

Remaining drugs are grouped into a fifth miscellaneous class.

1. Hypertension

TABLE 1a. Use of Medications for Control of Hypertension-Prevalence

Prescription drug classes included in this table are:

- •Diuretics (thiazide, loop, and potassium, sparing) (Class A)
- •Beta blockers (Class B)
- •Calcium-channel blockers (Class C)
- •ACE-inhibitors (Class D)
- •Other agents (including aldosterone receptor blockers, combined alpha and beta blockers, angiotensin II antagonists, $alpha_1$ blockers, central $alpha_2$ agonists, and direct vasodilators) (Class E)

	# of Class A Patients	# of Class B Patients	# of Class C Patients	# of Class D Patients	# of Class E Patients	# of Mult Class Patients	Total # of Patients on Any Class	# of Patients Per 1,000 Member Years
AGE								
0-4	243	57	73	118	131	103	501	4
5-9	78	87	36	71	566	48	778	8
10-17	240	320	156	161	816	103	1,560	11
18-34	3,297	2,863	2,078	2,432	1,757	2,223	9,467	41
35-44	6,452	3,947	2,827	5,606	3,083	5,507	14,476	141
45-54	13,444	7,477	5,825	12,001	7,096	13,135	27,509	296
55-64	13,739	7,619	6,376	11,674	8,065	14,547	26,152	503
65-84	8,025	4,292	3,831	5,875	4,099	8,252	13,193	681
85+	1,559	583	565	902	494	1,278	2,144	780
GENDER								
Male	17,229	12,576	9,846	20,551	13,377	20,870	42,902	103
Female	29,848	14,669	11,921	18,289	12,730	24,326	52,878	119
GEOGRAPHIC AREA								
Urban	34,781	20,029	16,419	29,117	19,600	33,617	71,367	135
Rural	12,296	7,216	5,348	9,723	6,507	11,579	24,413	74
TOTAL	47,077	27,245	21,767	38,840	26,107	45,196	95,780	111

1. Hypertension (cont)

TABLE 1b. Use of Medications for Control of Hypertension-Medication Possession Ratio (MPR)

Prescription drug classes included in this table are:

- •Diuretics (thiazide, loop, and potassium, sparing) (Class A)
- •Beta blockers (Class B)
- •Calcium-channel blockers (Class C)
- •ACE-inhibitors (Class D)
- •Other agents (including aldosterone receptor blockers, combined alpha and beta blockers, angiotensin II antagonists, $alpha_1$ blockers, central $alpha_2$ agonists, and direct vasodilators) (Class E)

MPR greater than .80 Adherent
MPR from .20 to .80 Partially adherent
MPR less than .20 Nonadherent

	MPR of Class A Patients	MPR of Class B Patients	MPR of Class C Patients	MPR of Class D Patients	MPR of Class E Patients	MPR of Patients on Mult Class	MPR of Patients on Any Class
AGE							
0-4	.74	.80	.72	.82	.79	.81	.78
5-9	.78	.84	.79	.84	.81	.91	.82
10-17	.80	.81	.80	.78	.81	.80	.80
18-34	.80	.81	.82	.81	.82	.81	.81
35-44	.81	.83	.84	.84	.83	.84	.83
45-54	.84	.84	.86	.85	.85	.87	.86
55-64	.85	.85	.87	.87	.87	.90	.88
65-84	.84	.85	.87	.87	.87	.90	.89
85+	.86	.86	.87	.87	.87	.92	.90
GENDER							
Male	.85	.85	.86	.86	.86	.88	.87
Female	.83	.84	.86	.86	.86	.88	.86
GEOGRAPHIC AREA							
Urban	.84	.84	.86	.86	.86	.88	.86
Rural	.84	.84	.86	.86	.86	.88	.86
TOTAL	.84	.84	.86	.86	.86	.88	.86

1. Hypertension (cont)

TABLE 1c. Use of Medications for Control of Hypertension-Persistence

Prescription drug classes included in this table are:

- •Diuretics (thiazide, loop, and potassium, sparing) (Class A)
- •Beta blockers (Class B)
- •Calcium-channel blockers (Class C)
- •ACE-inhibitors (Class D)
- •Other agents (including aldosterone receptor blockers, combined alpha and beta blockers, angiotensin II antagonists, $alpha_1$ blockers, central $alpha_2$ agonists, and direct vasodilators) (Class E)

The values in the table represent the median length of time (in days) a patient went without a drug.

	Median Days Without Drug For Class A Patients	Median Days Without Drug For Class B Patients	Median Days Without Drug For Class C Patients	Median Days Without Drug For Class D Patients	Median Days Without Drug For Class E Patients	Median Days Without Drug For Mult Class	Median Days Without Drug For Any Class
AGE							
0-4	15.3	8.00	17.4	11.2	14.6	12.0	12.6
5-9	12.0	8.00	9.00	7.82	9.42	5.00	9.00
10-17	10.6	11.5	9.90	13.0	10.0	13.1	10.3
18-34	10.7	9.00	8.67	9.25	8.73	10.0	9.67
35-44	9.00	7.43	7.40	7.60	8.33	8.00	8.33
45-54	8.00	7.00	6.50	6.60	7.00	6.83	7.00
55-64	7.50	6.67	6.00	6.33	6.33	6.00	6.50
65-84	9.07	8.20	7.00	7.29	7.69	7.00	7.50
85+	7.50	7.00	6.50	7.00	6.71	6.80	7.00
GENDER							
Male	7.75	7.19	6.67	6.80	7.13	6.75	7.00
Female	8.67	7.50	7.00	7.00	7.33	7.00	7.67
GEOGRAPHIC AREA							
Urban	8.00	7.20	6.75	7.00	7.13	6.88	7.20
Rural	8.67	8.00	7.00	7.00	7.50	7.17	7.71
TOTAL	8.23	7.40	6.83	7.00	7.25	7.00	7.33

Hypertension - Key Findings

Prevalence:

1) The rate of patients receiving a medication from one or more of the hypertension (high blood pressure) indicator drug classes is **111 patients/1000 member years.**

2) This rate for adults 18 and older is 186 patients/1000 member years. **This tends to increase with age**, with a rate for patients 65 and older of 780 patients/1000 member years. **This rate is also higher in women** (119 patients/1000 member years) than men (103 patients/1000 member years).

3) Roughly half of the patients (47%) receive combination therapy (more than one drug class).

4) **Diuretics** are the most common drug class prescribed, with 49% of patients receiving a diuretic.

5) 41% of patients receive an **ACE-inhibitor**, the next most frequently prescribed class.

Medication Possession Ratio (MPR):

1) The Medication Possession Ratio (MPR) for all five of the hypertension drug classes, as well as the overall MPR, is between .8 and .9 (indicating patient adherence). **While there are not significant differences among drug classes, MPR does tend to improve with age.**

Persistence:

1) For all five of the hypertension drug classes, the median length of time patients went without their drugs was between six and nine days.

Hypertension - Limitations

1) **Diagnosis information is not available in these records.** As many of the drugs used to treat hypertension are also used to treat other conditions such as congestive heart failure, **some patients whose data are analyzed in this indicator will not be receiving these drugs for hypertension**.

2) A number of less frequently prescribed drug classes were grouped together for analysis purposes into Class E, "Other agents". Patients receiving multiple drug types in Class E were only counted as receiving one drug class. Thus, **the overall percentage of patients receiving combination therapy is actually higher than 47%**.

3) Definite plan entry and exit dates for participants are not known. As such, decision rules used to calculate medication possession ratio and persistence will likely yield:

    - a higher (more favorable) MPR value than is the case
    - a lower (more favorable) persistence value than is the case

Hypertension - Discussion

Background

Hypertension is a "silent killer" that affects approximately 65 million, or 1 in every 3, Americans.[1] It is considered a silent killer because hypertension usually does not develop acute signs or symptoms, but has serious consequences when left untreated. Some of the long-term consequences include stroke, heart failure, end-stage renal disease, and coronary heart disease.[1] Although the prevalence of hypertension increases approximate 10% for every decade after age 45, it is not part of healthy growing and may be prevented with lifestyle changes and controlled with pharmacologic treatments.[2] Since the late 1970s, the awareness of hypertension among the general population as reported by survey data increased from 10%to 70%, but control of hypertension (defined as blood pressure level of 140/90 mm Hg) only increased from 10% - 34% despite the availability of newer pharmacologic therapies.[1]

The Healthy People 2010 objectives identified lowering the proportion of adults with high blood pressure and increasing the proportion of patients to be under control as one of the 12 major focus area.[3] The National High Blood Pressure Education Program presents the complete Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) which sets guidelines to meet these objectives. The report provides an evidence-based approach to the prevention and management of hypertension.[1]

Disease Classification

The classification of blood pressure is based on an average of 2 or more blood pressure readings during separate physician visits. The classification is strictly based on the blood pressure without regard to patient risk factors. The presence or absence of risk factors usually guides the choice and the intensity of the pharmacological treatment. The new guideline recommends pharmacological treatments for patients in stages 1 and 2 hypertension with a blood pressure goal <140/90 mmHg. Prehypertension is not a true disease state, but lifestyle modification is encouraged to return to the blood pressure goal of <140/90 mmHg. The systolic and diastolic blood pressures associated with disease classification are listed in Table 1.

Table 1. Classification of blood pressure for adults[1]

Blood Pressure Classification	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)
Normal	<120	and <80
Prehypertension	120 – 139	or <80-89
Stage 1 Hypertension	140 – 159	or <90-99
Stage 2 Hypertension	≥160	or ≥100

Pharmacological Treatment

Antihypertensive therapy has been associated with reduction of 35-40% in the incident of stroke, 20-25% in myocardial infarction, and >50% in heart failure.[4] Diuretics, angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), beta blockers (BBs), and calcium channel blockers (CCBs) are currently approved for treatment of hypertension (Table 2). Fixed combination therapies have been developed to increase compliance and adherence because majority of the patients with high blood pressure require more than 1 drug to achieve the blood pressure goal <140/90 mmHg.[5] The available combination therapies are listed in Table 3.

Table 2. Oral antihypertensive drugs[1]

Class	Generic (Brand) Name
Thiazide diuretics	Chlorothiazide (Diuril), Chlorthalidone (multiple generic), Hydrochlorothiazide (Microzide, HydroDIURIL), Polythiazide (Renese), Indapamide (Lozol), Metolazone (Mykrox, Zaroxolyn)
Loop diuretics	Bumetanide (Bumex), Furosemide (Lasix), Torsemide (Demadex)
Potassium-sparing diuretics	Amiloride (Midamor), Triamterene (Dyrenium)
Aldosterone receptor blockers	Eplerenone (Inspra), Spironolactone (Aldactone)
Beta blockers	Atenolol (Tenormin), Betaxolol (Kerlone), Bisoprolol (Zebeta), Metoprolol (Lopressor), Metoprolol extended release (Toprol XL), Nadolol (Corgard), Propranolol (Inderal), Propranolol long-acting (Inderal LA), Timolol (Blocadren)
Beta Blockers with Intrinsic Sympathomimetic Activity	Acebutolol (Sectral), Penbutolol (Levatol), Pindolol (generic)
Combined Alpha- and Beta-Blockers	Carvedilol (Coreg), Labetalol (Normodyne, Trandate)
Angiotensin Converting Enzyme Inhibitors	Benazepril (Lotensin), Captopril (Capoten), Enalapril (Vasotec), Fosinopril (Monopril), Lisinopril (Prinivil, Zestril), Moexipril (Univasc), Perindopril (Aceon), Quinapril (Accupril), Ramipril (Altace), Trandolapril (Mavik)
Angiotensin II Antagonists	Candesartan (Atacand), Eprosartan (Teveten), Irbesartan (Avapro), Losartan (Cozaar), Olmesartan (Benicar), Telmisartan (Micardis), Valsartan (Diovan)
Calcium Channel Blockers (nondihydropyridines)	Diltiazem extended release (Cardizem CD, Dilacor XR, Tiazac), Diltiazem extended release (Cardizem LA), Verapamil immediate release (Calan, Isoptin), Verapamil long acting (Calan SR, Isoptin SR), Verapamil (Coer, Covera HS, Verelan PM)

Class	Generic (Brand) Name
Calcium Channel Blockers (dihydropyridines)	Amlodipine (Norvasc), Felodipine (Plendil), Isradipine (Dynacirc CR), Nicardipine sustained release (Cardene SR), Nifedipine long-acting (Adalat CC, Procardia XL), Nisoldipine (Sular)
Alpha1 blockers	Doxazosin (Cardura), Prazosin (Minipress), Terazosin (Hytrin)
Central alpha2 agonists and other centrally acting drugs	Clonidine (Catapres), Clonidine patch (Catapres-TTS), methyldopa (Aldomet), Reserpine (generic), Guanfacine (Tenex)
Direct Vasodilators	Hydralazine (Apresoline), Minoxidil (Loniten)

*Adapted from JNC7

Table 3. Combination drugs for hypertension[1]

Class	Fixed Combination	Brand Name
ACEI and CCBs	Amlodipine-benazepril	Lotrel
	Enalapril-felodipine	Lexxel
	Trandolapril-verapamil	Tarka
ACEIs and diuretics	Benazepril-hydrochlorothiazide	Lotensin HCT
	Captopril-hydrochlorothiazide	Capozide
	Enalapril-hydrochlorothiazide	Vaseretic
	Fosinopril-hydrochlorothiazide	Monopril/HCT
	Lisinopril-hydrochlorothiazide	Prinzide, Zestoretic
	Moexipril-hydrochlorothiazide	Uniretic
	Quinapril-hydrochlorothiazide	Accuretic
ARBs and diuretics	Candesartan-hydrochlorothiazide	Atacand HCT
	Eprosartan-hydrochlorothiazide	Teveten-HCT
	Irbesartan-hydrochlorothiazide	Avalide
	Losartan-hydrochlorothiazide	Hyzaar
	Olmesartan medoxomil-hydrochlorothiazide	Benicar HCT
		Micardis-HCT
	Telmisartan-hydrochlorothiazide	Diovan-HCT
	Valsartan-hydrochlorothiazide	
BBs and diuretics	Atenolol-chlorthalidone	Tenoretic
	Bisoprolol-hydrochlorothiazide	Ziac
	Metoprolol-hydrochlorothiazide	Lopressor HCT
	Nadolol-bendroflumethiazide	Corzide
	Propranolol LA-hydrochlorothiazide	Inderide LA
	Timolol-hydrochlorothiazide	Timolide
Centrally acting drug and diuretic	Methyldopa-hydrochlorothiazide	Aldoril
	Reserpine-chlorthalidone	Demi-Regroton, Regroton
	Reserpine-chlorothiazide	Diupres
	Reserpine-hydrochlorothiazide	Hydropres
Diuretic and diuretic	Amiloride-hydrochlorothiazide	Moduretic
	Spironolactone-hydrochlorothiazide	Aldactazide
	Triamterene-hydrochlorothiazide	Dyazide, Maxzide

*Adapted from JNC7 Key: ACEIs=angiotensin converting enzyme inhibitors; ARBs=angiotensin receptor blockers; BBs=beta blockers; CCBs=calcium channel blockers

The current guideline recommends lifestyle modifications to prevent development of stage 1 or 2 hypertension without any pharmacologic treatments. Thiazide diuretics with or without drugs from another class (ACEIs, ARBs, BBs, CCBs) should be used for uncomplicated hypertension. Other specific therapies are indicated when the patient exhibits other high-risk conditions including heart failure, ischemic heart disease, chronic kidney disease, recurrent stroke, diabetes, and high coronary disease. Patients with diabetes, chronic kidney disease, and patients whose blood pressure is more than 20 mmHg above the systolic blood pressure goal or more than 10 mmHg above the diastolic blood pressure goal are recommended to take two or more antihypertensive medications. Previous clinical trials have indicated certain advantages in using certain classes of antihypertensive therapies as first line treatment. (Table 4)

Table 4. Drug classes used for high risk conditions in large clinical trials[1]

	Diuretics	BB	ACEI	ARB	CCB	AA
Heart failure	X	X	X			X
Postmyocardial infarction		X	X			X
High coronary disease risk	X	X	X		X	
Diabetes	X	X	X	X	X	
Chronic kidney disease			X	X		
Recurrent stroke prevention	X		X			

Key: AA=aldosterone antagonists; ACEIs=angiotensin converting enzyme inhibitors; ARBs=angiotensin receptor blockers; BBs=beta blockers; CCBs=calcium channel blockers

Adherence

Previous Studies

Regardless of therapy or care, the JNC7 guidelines emphasizes compliance to antihypertensive drug therapy is essential for hypertension control. The oral medications are labeled for 1-3 times per day and once per week for the patch. Previous compliance studies have focused on various drug therapy, depending on what was considered "first-line" treatment at the time the study was conducted.

Studies have shown that many patients are not compliant with their hypertensive drug therapy, a study of hypertensive patients in the New York Medicaid population showed that approximately 50% of the patients were not receiving adequate drug therapy.[6]

There were many hypotheses as to what would effect compliance for antihypertensive prescriptions, and like most other diseases non-compliance is multifactorial problem. One study attempted to determine the effects of an access restriction and found that after implementation of a preferred drug list, Medicaid patients were more likely to discontinue filling prescriptions for antihypertensive medication.[7] Regimen complexity does appear to effect compliance. A study showed that patients demonstrated longer persistence when controlled on fixed combination therapies than patients controlled on concurrent 2-pill therapy.[8] Most of the studies available examine compliance using different categories of antihypertensives, and few studies did head-to-head drug comparisons. One study suggested better persistence if patients were first start on ACEI.[9] Comparative trials between the use of amlodipine, lisinopril, or valsartan in usual setting suggested better persistence and compliance with valsartan.[10]

Table 5. Comparative trials for the rates of compliance measures from retrospective database studies of oral hypoglycemic agents

Study Year	Population Time	Treatment	N	Compliance	MPR	Persistence	Study Definitions
Wogen et al[10] 2001	PBM 1 year	Amlodipine Lisinopril Valsartan	73,148 40,128 29,669	86.7 ± 20.2 86.3 ± 20.5 88.5 ± 18.0	67.2 ± 0.14 64.6 ± 0.19 75.3 ± 0.22	53% 50% 63%	Compliance - Total days supply of all index medication prescriptions (excluding the days supply of the final prescription fill) divided by patient length of therapy, expressed as a percentage Persistence - Remaining on therapy with the index agent (did not discontinue index therapy prior to this time) MPR - Sum of the days supply for all index prescription fills during the 12 months subsequent to the index prescription divided by 365 days, expressed as a percentage of time that a patient had a supply of the index drug available during the 12 months following the index prescription
Caro et al [11] 1999	Saskatchewan Health in Canada (newly diagnosed) 6 months	ACEI CCB BB Diuretic	7,241 3,305 2,713 9,659			89% 86% 85% 80%	Persistence - if the last prescription filled during the study period provided sufficient medication to cover the period until the end of observation.

Key: ACEIs=angiotensin converting enzyme inhibitors; ARBs=angiotensin receptor blockers; BBs=beta blockers; CCBs=calcium channel blockers

Persistence Measures

Persistence measures were the main compliance outcome for the majority of studies examining antihypertensive use because hypertension is a chronic condition. Patients were regarded as persisting if they renewed their prescription within three times the number of days supplied by the previous prescription.[8] Other surrogate time measures of persistence include having had therapy available greater than 50% of the time[7] or having a duration of therapy >273 days[9] during a 12-month period.

Use of the Indicator

The Utah Heart Disease and Stroke Prevention Program proposed this indicator to determine the antihypertensive drugs most frequently prescribed hypertension. The usage trends could be used as a proxy to indicate what kinds of professional education might be needed to enhance or update provider knowledge to adhere to the JNC7 guidelines. The intervention programs will be based on improving guideline adherence and determine the most cost-effective agents within each category of antihypertensive therapies. Finally, long-term data can demonstrate the impact of compliance to therapies and increase provider awareness. The goal of this indicator is to influence provider practice in improving control of hypertension which would hopefully prevent future complications of congestive heart failure and acute myocardial infarction, ultimately impacting quality of life and decreasing premature mortality and morbidity.

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Indicator 2 - Diabetes

Diabetes - Introduction

Diabetes is a metabolic disorder where not enough insulin is produced or the body's cells do not respond appropriately to insulin. As a result glucose, which is used by cells for energy, builds up in the bloodstream resulting in high blood sugar levels.

Diabetes affects roughly eighteen million Americans, with roughly one-third of these people not yet diagnosed. The number of Americans with diabetes roughly doubled from 1980 through 2003 and projections call for the increase in diabetes prevalence to continue.

Type 1 diabetes is an autoimmune disease and develops most often in children and young adults. Type 2 diabetes is more common, affecting roughly ninety percent of patient suffering diabetes. It is associated with factor including increasing age, obesity, and family history. Finally, gestational diabetes occurs during pregnancy.

This indicator focuses on use of three major classes of drugs used to treat diabetes:

- Insulins
- Sulfonylureas
- Biguanids

Remaining drugs are grouped into a fourth miscellaneous class.

2. Diabetes

TABLE 2a. Use of Medications for Control of Diabetes-Prevalence

Prescription drug classes included in this table are:

- •Insulins (Class A)
- •Sulfonylureas (Class B)
- •Biguanides (Class C)
- •Other agents (including alpha-glucosidase inhibitors, meglitinides, thiazolidinediones, and combination agents) (Class D)

	# of Class A Patients	# of Class B Patients	# of Class C Patients	# of Class D Patients	# of Mult Class Patients	Total # of Patients on Any Class	# of Patients Per 1,000 Member Years
AGE							
0-4	97	1	2	3	1	102	1
5-9	266	2	7	1	2	274	3
10-17	798	15	212	17	66	970	7
18-34	2,268	535	2,514	471	668	4,938	21
35-44	1,467	1,274	2,741	1,133	1,489	4,603	45
45-54	2,122	3,126	4,689	2,500	3,470	7,724	83
55-64	2,035	3,453	4,591	2,639	3,716	7,670	148
65-84	1,361	2,102	1,979	1,329	1,926	4,171	215
85+	170	246	102	113	170	417	152
GENDER							
Male	5,133	5,448	7,096	4,017	5,603	14,047	34
Female	5,451	5,306	9,741	4,189	5,905	16,822	38
GEOGRAPHIC AREA							
Urban	7,969	8,087	12,855	6,275	8,763	23,365	44
Rural	2,615	2,667	3,982	1,931	2,745	7,504	23
TOTAL	10,584	10,754	16,837	8,206	11,508	30,869	36

2. Diabetes (cont)

TABLE 2b. Use of Medications for Control of Diabetes-Medication Possession Ratio (MPR)

Prescription drug classes included in this table are:

- •Insulins (Class A)
- •Sulfonylureas (Class B)
- •Biguanides (Class C)
- •Other agents (including alpha-glucosidase inhibitors, meglitinides, thiazolidinediones, and combination agents) (Class D)

MPR greater than .80 Adherent
MPR from .20 to .80 Partially adherent
MPR less than .20 Nonadherent

	MPR of Class A Patients	MPR of Class B Patients	MPR of Class C Patients	MPR of Class D Patients	MPR of Patients on Mult Class	MPR of Patients on Any Class
AGE						
0-4	.58	1.0	.76	1.0	1.0	.59
5-9	.57	.71	.84	1.0	1.0	.57
10-17	.65	.76	.74	.77	.76	.66
18-34	.63	.77	.77	.80	.76	.71
35-44	.62	.80	.80	.80	.83	.77
45-54	.62	.82	.82	.83	.85	.81
55-64	.62	.84	.84	.85	.87	.84
65-84	.55	.84	.85	.85	.86	.82
85+	.46	.87	.88	.88	.84	.82
GENDER						
Male	.62	.83	.83	.85	.86	.80
Female	.60	.83	.81	.83	.84	.79
GEOGRAPHIC AREA						
Urban	.62	.83	.82	.84	.86	.80
Rural	.59	.83	.82	.83	.84	.78
TOTAL	.61	.83	.82	.84	.85	.80

2. Diabetes (cont)

TABLE 2c. Use of Medications for Control of Diabetes-Persistence

ription drug classes included in this table are:

(Class A)
lureas (Class B)
ides (Class C)
alpha-glucosidase inhibitors, meglitinides, thiazolidinediones, and combination agents) (Class D)

values in the table represent the median length of time (in days) a patient went without a drug.

	Median Days Without Drug For Class A Patients	Median Days Without Drug For Class B Patients	Median Days Without Drug For Class C Patients	Median Days Without Drug For Class D Patients	Median Days Without Drug For Mult Class	Median Days Without Drug For Any Class
AGE						
0-4	29.9		29.0			30.0
5-9	24.3	13.3	9.92			24.1
10-17	19.1	9.50	13.2	14.0	14.3	18.0
18-34	20.0	11.8	13.0	10.0	13.4	16.5
35-44	20.7	9.60	10.0	9.50	9.23	12.3
45-54	20.7	8.67	8.38	8.00	8.33	9.87
55-64	20.8	8.00	7.33	7.00	7.94	9.00
65-84	22.7	8.50	8.75	8.13	9.00	10.0
85+	26.1	6.00	7.57	7.00	10.0	9.50
GENDER						
Male	20.4	8.00	8.00	7.60	8.20	11.0
Female	21.0	9.00	9.50	8.45	9.00	11.3
GEOGRAPHIC AREA						
Urban	20.7	8.50	9.00	8.00	8.67	11.0
Rural	21.3	8.50	9.14	8.40	9.00	11.7
TOTAL	20.9	8.50	9.00	8.00	8.75	11.0

Diabetes - Key Findings

Prevalence:

1) The **overall rate** of patients receiving a medication from one or more of the diabetes indicator drug classes is **36 patients per 1000 member years. This figure is significantly higher in adults 18 and over** (58 patients per 1000 member years) than patients under 18 years of age (4 patients per 1000 member years).

2) **Over one-third of patients (37%) receive combination therapy** (more than one drug class).

3) **Biguanides** are the most common drug class prescribed, with 55% of patients receiving a biguanide. This drug class includes Glucophage (metformin).

4) Patients are rather evenly split among the remaining three drug classes – **insulins, sufonylureas, and other agents**. Each of these classes is prescribed to between 25 and 35% of patients.

Medication Possession Ratio (MPR):

1) The Medication Possession Ratio (MPR) for three of the four diabetes drug classes is between .8 and .9 (indicating patient adherence). The MPR for insulins is lower at .61 but there are specific difficulties with MPR for insulins (see Limitations below).

Persistence:

1) As with the MPR, the median length of time patients went without their drugs for three of the four drug classes was quite similar (between eight and nine days). This value was higher for insulins (twenty-one days) but as with MPR, there are specific difficulties with insulins when calculating prevalence (see Limitations below).

Diabetes - Limitations

1) As opposed to other medication classes where a patient receives a set number of pills to take per day, **insulin doses can vary for each patient depending on a number of factors**. A 30 day supply filled by a pharmacist is thus an estimate – the fact a patient goes 40 days before refilling their insulin does not necessarily mean the patient was noncompliant. **As days supplied and days until next refill are the only data available to calculate MPR/persistence, these figures will likely appear worse (lower MPR, higher persistence) for insulin than is the case.**

2) **Diagnosis information is not available in these records**. This limitation is largely mitigated by the fact that drugs used to treat diabetes are relatively specific for this disease.

3) Definite plan entry and exit dates for participants are not known. As such, decision rules used to calculate medication possession ratio and persistence will likely yield:

    - a higher (more favorable) MPR value than is the case
    - a lower (more favorable) persistence value than is the case

Diabetes - Discussion

Background

Diabetes is estimated to affect 6.3% of Americans with approximately a third of these patients unaware of their condition.[1] Prevalence tends to increase with age - in 2003, the prevalence of diagnosed diabetes among people aged 65-74 (17.3%) was approximately 14 times that of people less than 45 years of age (1.2%).[26]

The prevalence among children between 12-19 years old is about 4.1 per 1,000.[2] The current information on national prevalence of childhood type 2 diabetes is incomplete; however several studies have attempted to examine the trend in specific communities and ethnic populations. These smaller studies suggested an increasing trend for type 2 diabetes among children and adolescents.[3] Depending on the study, the incidence of type 2 diabetes is increasing at varying degrees, and the prevalence of newly diagnosed type 2 diabetes ranged from 8-46%.[2] This trend represents a major concern because the burden of diabetes for individuals and the cost for lifetime treatment will increase the current estimates exponentially.

Acute manifestations of diabetes include life-threatening ketoacidosis and nonketotic hyperosmolar syndrome. However, long-term complications including retinopathy, nephropathy, and neuropathy increase patients' risk of blindness, kidney failure, heart disease, and amputation. Diabetes is the leading cause of blindness between the ages of 20-74 years, the leading cause for end-stage renal disease, and patients with diabetes are 2-4 times more likely to die from a stroke than patients without diabetes.[1] This translates to a societal cost of $132 billion ($92 billion from direct medical costs, $40 billion from disability, work loss, and premature mortality).[1] These estimates will continue to rise as the prevalence of diabetes increases among adults and will increase dramatically if the prevalence trends in children are not reversed.

The American Diabetes Association (ADA) issued their annual position statement published in the January Supplement of *Diabetes Care*. It contained the official perspective of the ADA for diabetes disease classification and treatment targets. The summaries of these statements are included and used as a guideline for this report.[4, 5] The ADA, however, does not provide guidelines regarding pharmacologic therapy. Pharmacotherapy summaries are derived from several publications.[6]

Disease Classification

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia as a result of abnormal insulin secretion, insulin action, or both.[4] The American Diabetes Association defines type 1 diabetes (previously termed as insulin-dependent diabetes or juvenile-onset diabetes) as patients with autoimmune ß-cell destruction resulting in absolute insulin deficiency.[4] Type 2 diabetes (previously termed as non-insulin dependent diabetes or adult-onset diabetes) includes patients with a combination of insulin resistance and insulin deficiency that require lifestyle interventions and treatment with exogenous agents.[4] Gestational diabetes mellitus is a broad term for expectant mothers that experience glucose intolerance during their pregnancy.[4] Finally, there is a group consisting of other genetic defects, diseases, or drug-/ chemical-induced etiologic causes of diabetes. Although there are several labels for different types of diabetes, it is more important to understand the pathogenesis of diabetes after diagnosis.[4] The ADA criteria for the diagnosis of diabetes mellitus are summarized in Table 1.[4]

Table 1. Criteria for the diagnosis of diabetes mellitus[4]

Symptoms of diabetes plus casual plasma glucose concentration ≥200 mg/dl (11.1 mmol/L).

- Casual is defined as any time of day without regard to time since last meal.
- The classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss.

or

Fasting plasma glucose levels ≥126 mg/dL (7.0 mmol/L).

- Fasting is defined as no caloric intake for at least 8 hours.

or

2-hour postload glucose ≥200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test.

- The test should be performed as described by World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.

In the absence of unequivocal hyperglycemia, these criteria should be confirmed by repeat testing on a different day. The third measure of oral glucose tolerance test is not recommended for routine clinical use.

Pharmacological Treatment and Diabetes Treatment Guidelines

The recommended preprandial plasma glucose level for nonpregnant individuals is between 90-130 mg/dL (5.0-7.2 mmol/L) and the postpradial plasma glucose measured 1-2 hours after the beginning of the meal should be less than 180 mg/dL (<10.0 mmol/L).[5] The guideline stresses that goals should be individualized especially for children, pregnant women, and elderly persons. Despite these recommended goals, there is no specific treatment algorithm proposed by the ADA because treatment of diabetes consists of lifestyle changes, pharmacological agents, and patient characteristics. The Utah Department of Health Diabetes Prevention and Control Program established the Diabetes Practice Recommendation, which includes algorithms for treatment of type 1 and type 2 diabetes to assist physicians in the care of Utahns. **These guidelines, including "Diabetes Practice Recommendations for Adults" and "Diabetes Management in Pregnancy", can be found at www.health.utah.gov/diabetes.**

The Department of Health diabetes indicator would provide information on the types of medications being presented and filled for people with diabetes. Additionally, this will provide valuable information on physician prescribing and treatment trends to determine if physicians are adopting the Diabetes Practice Recommendation. Finally, this will assist Utah Department of Health in tracking the adoption of new medications approved by the Food and Drug Administration.

Insulin

Exogenous insulin is essential to sustain life for patients with type 1 diabetes because these patients do not produce sufficient quantities of insulin necessary to maintain normal carbohydrate, protein, and fat metabolism. Some patients in advanced stages of type 2 diabetes may also require the use of insulin to supplement oral medications or use as monotherapy. Insulin is available in rapid-, short-, intermediate-, and long-acting types that are packaged be to be injected separately or in combinations. Formulations of predetermined proportions of intermediate- and short-acting mixtures are available with a composite onset and duration of action of the components with one peak of action.[6] The available agents and their descriptions are described in Table 2.

Table 2. Insulin formulation and description[6]

Type of Insulin	Examples	Onset of Action	Peak of Action	Duration of Action
Rapid-acting	Lispro	15 minutes	30-90 minutes	3-5 hours
	Aspart	15 minutes	40-50 minutes	3-5 hours
Short-acting	Regular	30-60 minutes	50-120 minutes	5-8 hours
Intermediate-acting	Lente	1-3 hours	8 hours	20 hours
	NPH	1-2.5 hours	7-15 hours	18-24 hours
Long-acting	Ultralente	4-8 hours	8-12 hours	36 hours
	Glargine	1 hour	None	24 hours

Oral agents

Oral antidiabetic agents are used only in patients with type 2 diabetes. Oral treatments are separated into hypoglycemic agents, which stimulate insulin secretion, and insulin sensitizers, which increase the body's sensitivity to insulin. Oral medications are broadly categorized into 5 general classes: sulfonylureas, meglitinides, biguanides, thiazolidinediones, and alpha-glucosidase inhibitors. (see Table 3). Recently, fixed combination dosage forms have been introduced into the market to increase compliance and decrease drug burden for patients requiring 2 types of oral therapies. (see Table 4).

Table 3. Oral hypoglycemic and antihyperglycemic agents and description[6]

Oral hypoglycemic agents

Sulfonylureas MOA: stimulate pancreatic secretion of insulin and improve pancreatic ß-cell function major difference is duration of action, limited effectiveness after 5 years		
Generic name	Brand name	Duration of action (h)
First generation		
Tolbutamide	Orinase®	6-12
Chlorpropamide	Diabinse®	60
Talazamide	Tolinase®	12-24
Acetohexamide	Dymelor®	12-18
Second generation – more potent and safer, but equally effective as first generation		
Glipizide	Glucotrol®	12
Glipizide-GITS	Glucotrol XL®	24
Glyburide	DiaBeta®, Micronase®	16-24
Glyburide (micronized)	Glynase®	12-24
Glimepiride	Amaryl®	24

Meglitinides MOA: stimulate pancreatic secretion of insulin		
Generic name	Brand name	Duration of action (h)
Repaglinide	Prandin®	4-6
Nateglinide	Starlix®	2-4

Insulin sensitizers – antihyperglycemic agents

Biguanides

MOA: increase hepatic sensitivity to insulin resulting in hepatic glucose production suppresion

Generic name	Brand name	Duration of action (h)
Metformin	Glucophage®	5-12
	Glucophage XR®	24

Thiazolidinediones

MOA: increase number and /or sensitivity of insulin receptors in muscle and adipose tissue

Generic name	Brand name	Duration of action (h)
Pioglitazone (approved w/ insulin)	Actos®	24-48
Rosiglitazone	Avandia®	15-25

Alpha-glucosidase inhibitors

MOA: inhibits intestinal absorption of complex carbohydrates

Generic name	Brand name	Duration of action (h)
Acarbose	Precose®	6
Miglitol	Glyset®	6

Key: MOA=mechanism of action

Table 4. Combination oral hypoglycemic therapies and description

Generic Combination	Rational	Brand Names
Sulfonylureas and metformin	The goal is to produce mealtime stimulation of endogenous insulin with sulfonylurea and decrease nocturnal gluconeogenesis with metformin while also limiting excessive weight gain and improving lipid profile.	Metaglip® Glucovance®
Thiazoledinedione and Metformin	Combining these two agents exert a synergistic effect on glycemic reduction.	Avandamet®

Adherence

Previous Studies

The natural progression and the complexity of diabetes require patients to be adherent to their treatment to prevent or delay chronic complications. All oral medications must be taken regularly 1- 4 times daily as appropriate. The choice and duration of each therapy depend on the physician and patient response. Adherence to antidiabetic therapy has been associated with economic savings and optimizing gylcosylated hemoglobin (A1c) level.[7] Previous studies support the use of prescription information to determine diabetes medication possession, adherence, and compliance to pharmacotherapy, and also determine physician practice patterns. These studies will also be a proxy for Utah data.

A meta-analysis demonstrated adherence to diabetes medical treatment is approximately 67.5%, a much lower rate than HIV disease (88.3%), arthritis (81.2%), and gastrointestinal disorders (80.4%).[8] A recent systematic review of 11 retrospective studies demonstrated that adherence rates with oral hypoglycemic medications range between 36-93% in patients treated for 6-24 months.[9] Open observational studies demonstrated a narrower range of 79-85% adherence rate during 6-36 months of observation.[9] More specifically, once-daily regimens had higher adherence rates than twice –daily regimens (61% vs. 52%), and monotherapy regimens had higher adherence rates than polytherapy regimens (49% vs. 36%). Seven reports demonstrated a wide range of persistence with oral hypoglycemic treatments between 16-80% in patients remaining on treatment for 6-24 months.[9] The results from earlier studies demonstrated a wide variance because of the various methods to calculate adherence and persistence. A summary of the studies examined by Cramer is presented in Table 5.[9]

Table 5. Rates of adherence and persistence from retrospective database studies of oral hypoglycemic agents (Adapted from Cramer et al[9])

Study Year	Population	Treatment	Follow-up (months)	N	Adherence rate	Persistence	Persistence (days)
Boccuzzi et al[10] 2001	PBO, new start	Metformin Sulfonylurea Troglitazone¥ AGI Repaglinide Total	12	19,295 52,813 5,273 885 1,232 79,498	76.4% 80.1% 83.0% 70.4% 69.8% 79.2%	60.3%* 56.2%* 43.2%* 31.1%* 48.1%* 55.9%*	83±71
Brown et al[11] 1999	HMO, new start	OHA + insulin	10 yr	693 all		70%†	
Catalan et al[12] 2001	Canada	Acarbose	12	216 social assistance 677 seniors		16%* 20%*	83 105
Ciechanowski et al[13] 2000	HMO, all	OHA + insulin	12	119 not depressed 121 depressed	93% 85%		
Dailey et al[14] 2001	Medicaid, new start	Monotherapy Polytherapy	18	37,431	49% 36%	36%* 22%*	
Dezii and Kawabata[15] 2002	PBO	Glipizide QD Glipizide BID	12	992	60.5% 52.0%	44.4% 35.8%	
Donnan et al[16] 2002	Scotland	Sulphonylurea Metformin	12	1321 528	31.3% > 90% 33.9% > 90%		
Evans et al[17] 2002	Scotland	Sulfonylurea Metformin	6	2,275 1,350	87% 83%		

Study Year	Population	Treatment	Follow-up (months)	N	Adherence rate	Persistence	Persistence (days)
Mellkian et al[18] 2002	PBO	Monotherapy Mono to combination Polytherapy Poly to combination	6 6	105 59	54% 77% 71% 87%		
Morningstar et al[19] 2002	Canada	OHA	36	3,358	86%		
Rajagopalan et al [20] 2003	PBO	OHA + insulin	24	195,400 all 28,001 new start	81% 81%		
Scheclman et al [21] 2002	Clinic	OHA + insulin	15	810	80 ± 21%		
Sclar et al[22] 1999	Medicaid	OHA	12	975		39%‡	
Spoelstra et al[23] 2003	Netherland	OHA	12	411	85 ± 15%		
Venturini et al[24] 1999	HMO	Sulfonylurea	24	786	83 ± 22%		

*Persistence for 12 months; †persistence for 24 months; ‡persistence for 6 months; ¥removed from the market; AGI=alpha-glucosidase inhibitor; BID=twice a day; HMO=health maintenance organization; OHA=oral hy poglycemic agent; PBO=pharmacy benefit organization; QD=once a day

Study Methods

Previous studies have excluded patients using insulin because claims data do not provide a feasible method to measure adherence to injectable medications.[7] However, one study found women self-report to intentionally omit insulin injections as the result of weight gain.[25] Although insulin compliance is a great concern for the treatment of diabetes, at the present time, this cannot be addressed using the current pharmacy claims database in Utah. This report will focus on oral hypoglycemic therapies. Numerous compliance and persistence measures have been used in previously published literature.[7, 10, 16, 17, 19] The following section summarizes these methods.

Compliance

1. Continuous measure of medication gaps (CMG)[7, 19] or continuous multiple interval measure of over-supply (CMOS)[19]

$$CMG = \frac{\text{Pr}\,oportion\_of\_days\_with\_gaps\_in\_medication\_refills}{Number\_of\_days\_in\_the\_observation\_period}$$

2. Medication possession ratio (MPR)[10, 16, 19]

$$MPR = \frac{\sum_{i=1}^{n}\left(DaysSupplied\right)_i}{DateFilled_n - DateFilled_1 + DaysSupplied_n}$$

3. Average adherence (AA)[17]

$$AA = \frac{\sum_{i=1}^{n}\left(DaysSupplied\right)_i \times 100}{Study\_Time}$$

Persistence

1. Persistence (yes/no) was based on patient refill behavior to support at least 1 day's supply of the index OHA at any time during the *n*th month post–index date with a 30-day window.[10]
2. Persistence was defined as the proportion in each cohort who renewed their initial dispensation during the study and within the permissible period (gap) between the prescribed end of the first dispensation and the date of the next dispensation. The permissible gap after the first dispensation was defined as half the duration of the index dispensation or 7 days, whichever was longer.[12]
3. Percentage of days in interruption by summing all days in interruption, defined as an episode in which a refill or subsequent prescription of oral hypoglycemics was overdue by more than 15 days and by more than 25% of the intended duration of use, and diving by the total number of days of intended treatment with oral hypoglycemics in 12 months.[13]

National Statistics

National statistics have shown that there are approximately 18 million Americans 20 years or older to suffer from diabetes.[1] The percentage of adults with diabetes was 2.2% among those aged 20–39 years, 9.7% among those aged 40–59 years, and 18.3% among those aged 60 years and older.[1] Approximately 8.7% of men (8.7 million Americans) and women (9.3 million) aged 20 years or older have diabetes.[1] Among these adults, 19% use insulin and 53% take oral medications as their sole treatment, 12% require a combination of insulin and oral medications, and 15% do not take any medications for the treatment of diabetes.[1]

Future Studies

This indicator may be used to determine whether recommended medication use changes over time as the Practice Recommendations become accepted and implemented. The Program will then be able to determine whether more training on the Practice Recommendations is needed, or if additional research on medication management barriers should be considered. If diagnosis data become available, the Program would also like to track co-morbidity medication use.

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Indicator 3 - Hypercholesterolemia

Hypercholesterolemia - Introduction

Cholesterol is a fat found in the body and is used for energy and as a building block for cells. Hypercholesterolemia refers to elevated levels of cholesterol (total cholesterol and LDL cholesterol (the "bad" cholesterol)). Hypercholesterolemia is a risk factor for coronary heart disease.

Cardiovascular risk tends to increase with higher levels of blood cholesterol – that is, the higher the blood cholesterol, the higher the cardiovascular risk. While hypercholesterolemia can run in families, other lifestyle risk factors like diet have a large influence as well.

This indicator focuses on five classes of drug used to treat hypercholesterolemia:

- Statins
- Bile acid resins
- Fibric acid derivatives
- Antilipemic agents
- Cholesterol absorption inhibitors

3. Hypercholesterolemia

TABLE 3a. Use of Medications for Control of Hypercholesterolemia-Prevalence

Prescription drug classes included in this table are:

- •Statins (Class A)
- •Bile acid resins (Class B)
- •Fibric acid derivatives (Class C)
- •Antilipemic agents (Niacin) (Class D)
- •Cholesterol absorption inhibitors (Class E)

	# of Class A Patients	# of Class B Patients	# of Class C Patients	# of Class D Patients	# of Class E Patients	# of Mult Class Patients	Total # of Patients on Any Class	# of Patients Per 1,000 Member Years
AGE								
0-4	6	69			1	1	75	1
5-9	7						7	0
10-17	56	9	11	6	3	7	77	1
18-34	1,770	167	358	58	76	154	2,258	10
35-44	5,566	206	1,150	184	203	573	6,698	65
45-54	13,200	292	1,964	488	475	1,404	14,893	160
55-64	13,693	347	1,732	504	461	1,354	15,261	294
65-84	5,751	163	620	165	120	508	6,276	324
85+	327	23	18	3	2	9	363	132
GENDER								
Male	22,487	528	3,689	1,032	760	2,610	25,655	61
Female	17,889	748	2,164	376	581	1,400	20,253	46
GEOGRAPHIC AREA								
Urban	30,831	977	4,568	1,130	1,066	3,188	35,106	66
Rural	9,545	299	1,285	278	275	822	10,802	33
TOTAL	40,376	1,276	5,853	1,408	1,341	4,010	45,908	53

3. Hypercholesterolemia (cont)

TABLE 3b. Use of Medications for Control of Hypercholesterolemia-Medication Possession Ratio (MPR)

Prescription drug classes included in this table are:

- •Statins (Class A)
- •Bile acid resins (Class B)
- •Fibric acid derivatives (Class C)
- •Antilipemic agents (Niacin) (Class D)
- •Cholesterol absorption inhibitors (Class E)

MPR greater than .80 Adherent
MPR from .20 to .80 Partially adherent
MPR less than .20 Nonadherent

	MPR of Class A Patients	MPR of Class B Patients	MPR of Class C Patients	MPR of Class D Patients	MPR of Class E Patients	MPR of Patients on Mult Class	MPR of Patients on Any Class
AGE							
0-4	.79	.70			.82	.99	.73
5-9	.75						.75
10-17	.80	.69	.83	.97	.47	.79	.79
18-34	.79	.70	.77	.85	.85	.81	.79
35-44	.81	.72	.81	.83	.87	.83	.81
45-54	.83	.71	.84	.83	.87	.84	.83
55-64	.84	.72	.85	.86	.88	.87	.85
65-84	.85	.70	.86	.89	.87	.87	.85
85+	.85	.65	.85	1.0	.77	.85	.84
GENDER							
Male	.84	.74	.84	.86	.87	.86	.84
Female	.83	.68	.83	.85	.87	.84	.83
GEOGRAPHIC AREA							
Urban	.83	.72	.84	.86	.87	.85	.83
Rural	.84	.66	.83	.84	.87	.86	.83
TOTAL	.83	.71	.84	.85	.87	.85	.83

3. Hypercholesterolemia (cont)

TABLE 3c. Use of Medications for Control of Hypercholesterolemia-Persistence

Prescription drug classes included in this table are:

- •Statins (Class A)
- •Bile acid resins (Class B)
- •Fibric acid derivatives (Class C)
- •Antilipemic agents (Niacin) (Class D)
- •Cholesterol absorption inhibitors (Class E)

The values in the table represent the median length of time (in days) a patient went without a drug.

	Median Days Without Drug For Class A Patients	Median Days Without Drug For Class B Patients	Median Days Without Drug For Class C Patients	Median Days Without Drug For Class D Patients	Median Days Without Drug For Class E Patients	Median Days Without Drug For Mult Class	Median Days Without Drug For Any Class
AGE							
0-4	17.7	43.0			20.0	1.00	26.0
5-9	17.0						17.0
10-17	10.5	59.5	8.00	3.67	130	12.7	11.6
18-34	10.5	26.0	11.0	14.8	7.00	11.3	11.0
35-44	9.00	30.0	9.59	8.00	7.50	9.67	9.33
45-54	8.50	18.3	7.33	9.00	7.00	8.80	8.50
55-64	7.83	18.0	7.20	7.50	5.88	8.43	7.88
65-84	8.60	21.0	9.00	8.00	9.00	8.90	8.75
85+	7.88	18.0	8.80		10.3	4.80	8.25
GENDER							
Male	8.20	16.4	8.00	8.00	6.75	8.50	8.22
Female	8.75	25.0	8.33	8.00	6.67	9.67	9.00
GEOGRAPHIC AREA							
Urban	8.40	19.1	8.00	8.00	6.75	8.88	8.50
Rural	8.71	24.3	8.33	8.47	6.50	8.75	9.00
TOTAL	8.50	21.0	8.00	8.00	6.67	8.82	8.50

Hypercholesterolemia - Key Findings

Prevalence:

1) The **overall rate** of patients receiving a medication from one or more of the hypercholesterolemia (high cholesterol) indicator drug classes is **53 patients per 1000 member years.**

2) **This rate is 33% higher in males than females** (61 patients per 1000 member years and 46 patients per 1000 member years, respectively).

3) **The majority of patients are treated with only one drug class**. Only 9% of patients are on combination therapy.

4) **Statins** are by far the most common drug class prescribed, with 88% of patients receiving a statin.

5) **Only 2% of patients receiving statins are also on niacin.**

Medication Possession Ratio (MPR):

1) The Medication Possession Ratio (MPR) for four of the five hypercholesterolemia drug classes, as well as the overall MPR, is between .8 and .9 (indicating patient adherence). However, **the MPR for bile acid resins such as cholestyramine (Questran) and colestipol (Colestid) is only .71**, with lower MPR for rural patients (.66) and women (.68).

2) Overall MPR is similar for male/female patients and urban/rural patients.

Persistence:

1) For statins, fibric acid derivatives, antilipemic agents and cholesterol absorption inhibitors, the median length of time patients went without their drugs was between six and nine days. **This number is significantly higher for bile acid resins (twenty-one days).**

Hypercholesterolemia - Limitations

1) **Diagnosis information is not available in these records**. This limitation is largely mitigated by the fact that drugs used to treat hypercholesterolemia are relatively specific for this disease.

2) Definite plan entry and exit dates for participants are not known. As such, decision rules used to calculate medication possession ratio and persistence will likely yield:

    - a higher (more favorable) MPR value than is the case
    - a lower (more favorable) persistence value than is the case

Hypercholesterolemia - Discussion

Background

Coronary heart disease (CHD) is the leading cause of death in the industrialized world[1], and the burden continues to increase. Hypercholesterolemia (i.e., elevated levels of total cholesterol and low density lipoprotein cholesterol (LDL-C)) is a well recognized risk factor for CHD[2] and the benefits of lipid-lowering therapy for the prevention of cardiovascular complications are well documented.[3, 4] Observational studies indicate a continuous and positive log-linear relationship between plasma cholesterol levels and cardiovascular risk.[5] The relationship is approximately linear, implying that the proportion reduction in relative risk is similar throughout the range of cholesterol levels.

Disease Classification

Cholesterol is a fat-like substance (lipid) that is present in cell membranes and is a precursor of bile acids and steroid hormones. Cholesterol moves through the blood in distinct particles containing both lipids and proteins (lipoproteins). Three major classes of lipoproteins are found in the serum of fasting individuals: low density lipoproteins (LDL), high density lipoproteins (HDL), and very low density lipoproteins (VLDL). LDL cholesterol typically makes up 60-70% of total serum cholesterol and it is the major atherogenic lipoprotein and has long been identified as the primary target of cholesterol-lowering therapy. HDL cholesterol normally makes up 20-30% of total serum cholesterol. HDL levels, on the other hand, are inversely correlated with risk for CHD. The VLDL are triglyceride-rich lipoproteins, but contain 10-15% of the total serum cholesterol. VLDLs are produced by the liver and are precursors of LDL; some forms of VLDL appear to promote atherosclerosis, similar to LDL.

A common form of dyslipidemia is characterized by three lipid abnormalities: elevated triglycerides, small LDL particles and reduced HDL cholesterol.[6] Often the

lipoprotein concentrations in the lipid triad are not categorically abnormal, but are only marginally deranged. The lipid triad (i.e., atherogenic dyslipidemia) occurs commonly in persons with premature CHD.[7] Atherogenic dyslipidemia is a common component of the metabolic syndrome (insulin resistance, obesity, physical inactivity, high blood pressure). Most therapies that lower triglyceride or raise HDL cholesterol actually modify all of the components of the lipid triad.[4]

Multiple lines of evidence from experimental animal, epidemiology, and controlled clinical trials indicate a strong causal relationship between elevated LDL cholesterol and CHD.[4] Clinical intervention with LDL-lowering therapy in patients with advanced coronary atherosclerosis aims to stabilize plaques and to prevent acute coronary syndromes.[8] In contrast, LDL lowering earlier in life slows atherosclerotic plaque development, the foundation of the unstable plaque. This fact provides the rationale for long-term lowering of LDL cholesterol using both public-health and clinical approaches.[4] Other lipid risk factors that are secondary targets for therapy include triglycerides and HDL, the classification of lipid-related conditions is presented in Table 1.

Table 1. Initial classification cholesterol and triglycerides (not considering patient risk for CHD)

Classification	Total cholesterol (mg/dL)	LDL-cholesterol (mg/dL)	HDL-cholesterol (mg/dL)	Triglycerides (mg/dL)
Optimal/normal	< 200	<100	–	–
Near optimal	–	100-129	–	<150
Borderline High	200-239	130-159	–	150-199
High	≥240	160-189	>60	200-499
Very High	–	≥190	–	≥500
Low	–	–	<40	–

Key: CHD= Coronary heart disease; HDL= high density lipoproteins; LDL= low density lipoproteins

Lipid risk factors are the primary targets for CHD reduction and prevention; however, a number of nonlipid risk factors are also strongly associated with CHD risk and need to be considered when developing a cholesterol lowering or CHD prevention plan. Nonlipid risk factors can be classified as modifiable and nonmodifiable. Modifiable risk factors include hypertension, cigarette smoking, thrombogenic/hemostatic state, diabetes, obesity, physical inactivity, and atherogenic diet. Nonmodifiable risk factors include age, male gender, and family history of premature CHD.[4]

Pharmacological Treatment

LDL cholesterol is the primary target of treatment in clinical lipid management. The use of therapeutic lifestyle changes, including LDL-lowering dietary options and exercise will achieve the therapeutic goal in many persons. Nonetheless, a significant proportion of the population whose short-term and/or long-term risk for CHD will require LDL-lowering drug therapy in combination with lifestyle changes to reach the LDL cholesterol goal. HMG CoA reductase inhibitors (statins) support attainment of LDL goals in higher risk persons. Other agents – bile acid sequestrates, nicotinic acid, and some fibrates – are able to moderately lower LDL levels (Table 2).

Table 2. Lipid Lowering Medications: Average Effects on Cholesterol and Dose Range

Class	Lipid / lipoprotein effects	Available drugs Generic (Brand) name	Usual Starting Dose	Maximum Daily Dose
HMG CoA Reductase Inhibitors	LDL - ↓18-55% HDL - ↑5-15% TG - ↓7-30%	Lovastatin (Mevacor®)	20 mg	80 mg*
		Pravastatin (Pravachol®)	20 mg	80 mg*
		Simvastatin (Zocor®)	20 mg	80 mg*
		Fluvastatin (Lescol®)	20 mg	80 mg*
		Fluvastatin XL (Lescol XL®)	80 mg	80 mg*
		Atorvastatin (Lipitor®)	10 mg	80 mg*
		Rosuvastatin (Crestor®)	5 mg	40 mg*
Bile Acid Sequestrants	LDL - ↓15-30% HDL - ↑3-5% TG - no effect or ↑	Cholestyramine (Questran®, Prevalite®)	4-16 g	24 g
		Cholestyramine "light" (Questran Light®)	4-16 g	24 g
		Colestipol (Colestid®)	5-20 g	30 g
		Colesevelam (Welchol®)	2.6-3.8 g	4.4 g
Nicotinic Acid	LDL - ↓5-25% HDL - ↑15-35% TG - ↓20-50%	Crystalline nicotinic acid (Niasin®)	1.5-3 g	4.5 g
		Sustained-release nicotinic acid (Niasin®)	1-2 g	2 g
		Extended-release nicotinic acid (Niaspan®)	1-2 g	2 g
Fibric Acid Derivatives	LDL - ↓5-20% HDL - ↑10-35% TG - ↓20-50%	Gemfibrozil (Lopid®)	600 mg BID	1200 mg
		Fenofibrate (Tricor®)	200 mg	200 mg
		Clofibrate (Atromid-S®)	1000 mg BID	2000 mg
Selective Inhibitor of Intestinal Cholesterol	LDL - ↓15-18% HDL - ↑3% TG - no effect	Ezetimibe (Zetia®)	10 mg	10 mg
Combination Therapy	LDL - ↓ 53% HDL - ↑7% TG - ↓24%	Ezetimibe/simvastatin (Vytorin®)	10 mg/20mg	10 mg/80 mg
	LDL - ↓ 42% HDL - ↑30% TG - ↓44%	Lovistatin/niacin extended-release (Advicor®)	500 mg/20 mg	2000 mg/40 mg
	LDL - ↓ 31% HDL - ↑ 5% TG - ↓11%	Aspirin and pravastatin (Pravigard®)	81 or 325mg /40mg	325mg /80mg
	LDL - ↓39-60% HDL - ↑5-9% TG - ↓19-37%%	Amlodipine besylate/atorvastatin calcium (Caduet®)	10mg/10 mg	10mg / 80mg

* Maximum FDA-approved dose
Key: BID=twice a day; HDL=High-density lipoprotein; HMG CoA= Hydroxymethyl glutaryl coenzyme A; LDL=Low-density lipoprotein; NR=not reported in package insert; TG=triglyceride

A basic principle of prevention is that the intensity of risk-reduction therapy should be adjusted to a person's absolute risk for CHD. Risk assessment required measurement of LDL cholesterol as part of a lipoprotein analysis and identification of accompanying nolipid risks. According to the ATP III[1] algorithm[4, 9], persons are categorized into 3 risk categories: (1) established CHD and CHD risk equivalents[2], (2) multiple (2+) risk factors[3], and (3) zero to one risk factors. CHD risk equivalents include noncoronary forms of clinical atherosclerotic disease, diabetes, and multiple (2+) CHD risk factors with 10-year risk for CHD >20%. Having CHD or a risk equivalent is considered high risk. ATP III recommended that Framingham risk scoring be carried out in individuals with 2+ risk factors to triage them into 3 levels of 10-year risk for hard CHD events (myocardial infarction and CHD death): >20%, 10%-20%, and <10%. See table 3 for risk categories and ATP III updated treatment recommendations.[9]

[1] ATP III is the Adult Treatment Panel III, they are the panel that produced the third report of the National Cholesterol Education Program.
[2] CHD risk equivalents carry a risk for coronary events equal to that of established CHD, i.e., >20% per 10 years. CHD risk equivalents include: other clinical forms of atherosclerotic diseases (peripheral arterial disease, abdominal aortic aneurysm, and symptomatic carotid artery disease), diabetes and multiple risk factors that confer a 10-year risk for CHD >20%.
[3] Major risk factors (excluding LDL cholesterol) include: cigarette smoking, hypertension or antihypertensive medication, low HDL cholesterol (<40 mg/dL), family history of premature CHD, and age over 45 for males and 55 for females.

Table 3. LDL-C Goals and Cutpoints for TLC and Drug Therapy in Different Risk Categories (Modified ATP III Recommendations)[9]

Risk Category	LDL-C Goal	Initiate TLC	Consider Drug Therapy*
High risk: CHD or CHD risk equivalent (10-year risk >20%)	<100 mg/dL (optimal: <70 mg/dL)†	≥100 mg/dL	≥100 mg/dL‡ (< 100 mg/dL: consider)**
Moderately high risk: 2+ risk factor (10-year risk 10-20%)	<130 mg/dL (optimal: <100 mg/dL)	≥130 mg/dL	≥130 mg/dL (100-129 mg/dL: consider)∞
Moderate risk: 2+ risk factors (10-year risk <10%)	<130 mg/dL	≥130 mg/dL	≥160 mg/dL
Lower risk: 0-1 risk factor	<160 mg/dL	≥160 mg/dL	≥190 mg/dL (160-189 mg/dL: optional)

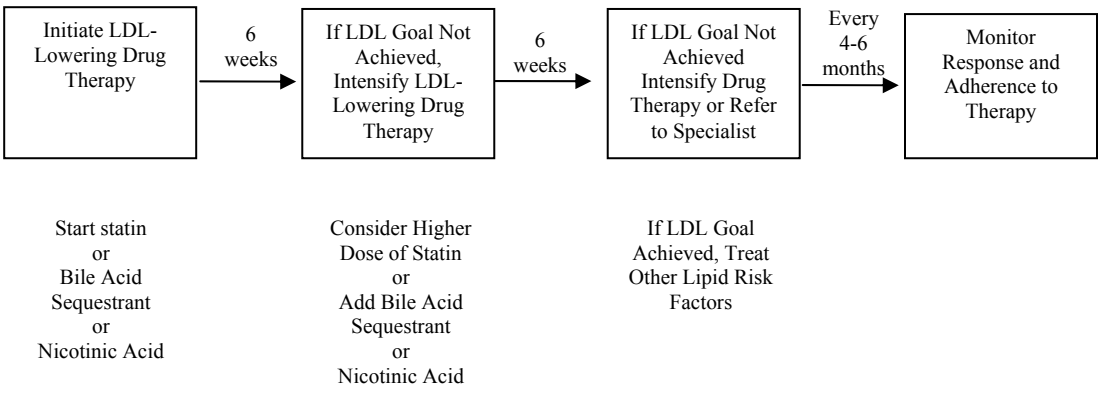
*When LDL-lowering therapy is employed, it is advised that intensity of therapy should sufficient to achieve at least a 30 to 40% reduction in LDL-C levels.

†Very high risk favors the optional LDL-C goal of <70 mg/dL, and in patients with high triglycerides, non-HDL-C <100 mg/dL

‡If baseline LDL-C is <100 mg/dL, institution of an LDL-lowering drug is a therapeutic option on the basis of available clinical trial results, If a high-risk person has high triglycerides or low HDL-C, combining a fibrate or nicotinic acid with and LDL-lowering agent can be considered.

∞For moderately high-risk persons, when LDL-C is 100 to 129 mg/dL, at baseline or on lifestyle therapy, initiation of an LDL-lowering drug to achieve and LDL-C level <100 mg/dL is a therapeutic option on the basis of available clinical trial results

Figure 1. Progression of Drug Therapy in Primary Prevention[4]



New Evidence not Included in NCEP Guidelines with Important Clinical Impact

Findings from the Arterial Biology for the Investigation of the Treatment Effects of Reducing cholesterol (ARBITER) 2 study was the first to demonstrate the incremental benefit of adding extended release niacin to statin therapy.[10] Statins are primarily designed to lower LCL-C while niacin is the most effect therapy for the treatment of low HDL-C. Combination therapy showed an incremental independent effect to retard the progression of atherosclerosis. The author's concluded that their study provides strong preliminary support for the expanded present clinical use of prescription extended-release niacin-statin therapy in combination for secondary prevention of CHD.

Adherence

The ATP III recommendations were largely based on clinical trial data, where the clinical utility of lipid-lowering regimens in reducing cardiac morbidity and mortality are well established. These studies tell us little of how lipid-lowering agents are being used in the natural setting. Developing a better understanding of lipid-lowering medication use throughout the health care system requires evaluating filled prescription rates as well as adherence to these drug therapies. Lack of persistent use of a medication for a chronic condition may result from patient noncompliance or from a physician's decision to discontinue therapy if adverse effects are believed to outweigh benefits.[11] Studies have shown that patients often are not prescribed lipid-lowering medications when they are indicated[12] and even fewer actually achieve serum cholesterol goals.[13]

Table 4. Rates of Adherence and Persistence from Retrospective Database Studies

Study Year	Population	Treatment	Follow-up (months)	N	Adherence rate	Persistence	Persistence (days)
Benner et al[14] 2002	NJ Medicaid and PAAD*	Statins	1990-1999 (1-9 yrs)	34,501		60%** 43% 26% 32%	90 180 1800 3600
Jackevicius et al[15] 2002	Claims data Ontario (≥66 years)	Statins	1994-1998	11.1 mill	ACS(40%)† CAD(36%) PP (25%)	ACS CAD PP 78% 75% 58% 60% 58% 38% 45% 40% 21%	 180 365 730
Avorn et al[11] 1998	NJ Medicaid and PAAD* Quebec (10% sample; ≥65 years)	All lipid-lowering drugs	12 months 1990-1991	5611 1676		NJ (59%) QC (63%)	365 or death

*PAAD = pharmaceutical assistance to the aged and disabled

** Proportion of population adherent at specific time period, proportion of days covered must be 80% or higher to be considered adherent during the time interval..

†Crude proportion of patients receiving statin prescriptions continuously for 2-years

Key: ACS=acute coronary syndrome; CAD=coronary artery disease; mill= million; NJ=New Jersey; QC=QuebecPP=primary prevention (PP)

••Estimated from survival curves (actual values were not presented in table)

Study Methods

Benner et al. evaluated statin use for up to 10 years after treatment was initiated.[14] They used the term "adherence" to represent the degree of prescription-filling in a given interval, and "persistence" to represent the duration of time over (in intervals) which a patient continued to fill statin prescriptions. Adherence was calculated for various time intervals and the proportion adherent was evaluated for each interval. Adherent individuals were defined as those with a proportion of days covered (PDC) of at least 80% in a given interval. Partially adherent individuals were those having a PDC of 20% to 79%; those with a PDC less than 20% were considered nonadherent.

Proportion of days covered (PDC):

$$PDC = \frac{\sum_{i=1}^{n} (DaysSupplied)_i}{(DateFilled_n - DateFilled_i) + DaysSupplied_n}$$

Jackevicius et al. compared long-term adherence and persistence between patients with acute and chronic coronary artery disease (secondary prevention) vs those without prior CAD (primary prevention) for a 2-year period after initiating a statin.[15] The primary outcome of adherence was defined as having a statin prescription dispensed at least every 120 days after the index prescription date until the end of the 2-year monitoring period. Patients receiving prescriptions in Ontario program may obtain a max of 100 days therapy with 1 prescription. One hundred and twenty days was chosen as the target refill to allow a 20% grace period for prescription refills. Duration of adherence was the difference between the index date and the final consecutive prescription date plus 90 days. Persistence was evaluated by comparing adherence rates at 180, 365, 545 and 730 days.

Avorn et al.,[11] measured adherence by determining the number of days a patient had lipid-reducing medication during the 365-day study. In both the United States and Canada, the highest compliance was associated with the use of statins (64.3% ± 29.8% of days covered), while the lowest was associated with cholestyramine (36.6% ± 29.1%). In

the US, patients who were prescribed a statin had an odds ratio for good persistence of about double that seen in patients prescribed other lipid-lowering agents.

National statistics

Cardiovascular disease accounts for 950,000 deaths annually in the United States, including 460,000 deaths from CHD. Elevated cholesterol is a major contributor to CHD. A sample of the US population from 1988-1999 indicates found the average total serum cholesterol levels for all age groups greater than 35 years old was over 200 mg/dL.[4]

Application

The lipid-lowering drug therapy indicator will help determine the prevalence of hypercholesterolemia in the state. Most importantly, this indicator will allow users to evaluate adherence and persistence with lipid-lowering agents and also compare these compliance rates to previous studies from other states. A better understanding of populations that are less compliant with their lipid-lowering medication will help the Department of Health plan strategies to support the appropriate use of lipid-lowering agents for the state of Utah. The state will also have an opportunity to evaluate changes in prescribing patterns of statin/niacin combination therapy in response to the ARBITER 2 trial. Slow adopters can be targeted for education on the benefits of combination therapy.

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Indicator 4 - Asthma

Asthma - Introduction

Asthma is a chronic airway disease and is one of the most common diseases worldwide. Symptoms can include wheezing, shortness of breath, and coughing. These are caused by a number of mechanisms (inflammation, airway constriction, mucus plugs) that then lead to airway obstruction. The list of asthma triggers is long and includes dust mites, animal dander, exercise, and certain medications.

The goal of asthma treatment is to control symptoms and prevent acute asthma attacks. While patients can go for long periods of time without asthma attacks (or milder symptoms), airway inflammation tends to be present on a chronic basis.

This indicator focuses on six classes of medications used for long-term control as well as medications used for quick relief of acute asthma attacks.

4. Asthma

TABLE 4a. Use of Medications for Control of Asthma-Prevalence

Prescription drug classes included in this table are:

- •Inhaled corticosteroids (Class A)
- •Cromolyn sodium and nedocromil (Class B)
- •Methylxanthines (Class C)
- •Leukotriene modifiers (Class D)
- •Antimuscarinic agents (Class E)
- •Long acting beta-agonists (inhaled and tablet) (Class F)
- •Short-acting beta-agonists (inhaled) (Class G)

	# of Class A Patients	# of Class B Patients	# of Class C Patients	# of Class D Patients	# of Class E Patients	# of Class F Patients	# of Class G Patients	# of Mult Class Patients	Total # of Patients on Any Class	# of Patients Per 1,000 Member Years
AGE										
0-4	3,642	33	1	1,973	403	3,959	10,010	4,121	14,740	125
5-9	2,585	37	2	2,088	123	1,707	4,908	2,838	7,247	73
10-17	3,786	50	8	2,173	204	2,983	8,137	4,194	10,704	76
18-34	4,705	34	86	1,670	537	4,766	10,457	5,138	14,228	61
35-44	3,594	20	117	1,323	635	3,168	5,987	3,945	8,384	81
45-54	4,115	27	203	1,563	1,059	3,494	5,400	4,522	8,371	90
55-64	3,072	25	274	1,062	1,216	2,563	3,540	3,475	5,718	110
65-84	1,425	7	156	450	992	1,202	1,900	1,890	2,855	147
85+	131		9	59	146	101	250	208	363	132
GENDER										
Male	12,377	111	340	5,670	2,257	10,534	23,742	13,869	33,686	81
Female	14,678	122	516	6,691	3,058	13,409	26,847	16,462	38,924	88
GEOGRAPHIC AREA										
Urban	20,827	162	602	8,905	3,705	18,019	38,401	22,953	54,551	103
Rural	6,228	71	254	3,456	1,610	5,924	12,188	7,378	18,059	54
TOTAL	27,055	233	856	12,361	5,315	23,943	50,589	30,331	72,610	84

Use of short-acting beta-agonists (rescue meds) is examined in Table 4D

4. Asthma (cont)

TABLE 4b. Use of Medications for Control of Asthma-Medication Possession Ratio (MPR)

Prescription drug classes included in this table are:

- •Inhaled corticosteroids (Class A)
- •Cromolyn sodium and nedocromil (Class B)
- •Methylxanthines (Class C)
- •Leukotriene modifiers (Class D)
- •Antimuscarinic agents (Class E)
- •Long acting beta-agonists (inhaled and tablet) (Class F)

MPR greater than .80 Adherent
MPR from .20 to .80 Partially adherent
MPR less than .20 Nonadherent

	MPR of Class A Patients	MPR of Class B Patients	MPR of Class C Patients	MPR of Class D Patients	MPR of Class E Patients	MPR of Class F Patients	MPR of Patients on Mult Class	MPR of Patients on Any Class
AGE								
0-4	.57	.65	1.0	.74	.59	.61	.59	.62
5-9	.58	.67	1.0	.72	.63	.62	.66	.66
10-17	.62	.48	.73	.72	.65	.65	.66	.66
18-34	.65	.67	.83	.80	.60	.68	.68	.70
35-44	.64	.52	.77	.81	.56	.68	.70	.70
45-54	.65	.51	.80	.82	.58	.69	.72	.71
55-64	.66	.54	.84	.86	.61	.71	.75	.73
65-84	.65	.44	.89	.86	.55	.71	.73	.70
85+	.58		.76	.92	.48	.66	.73	.68
GENDER								
Male	.63	.59	.84	.77	.60	.68	.69	.68
Female	.64	.54	.82	.80	.57	.68	.71	.70
GEOGRAPHIC AREA								
Urban	.63	.57	.83	.78	.58	.68	.70	.69
Rural	.63	.54	.82	.78	.58	.67	.69	.69
TOTAL	.63	.56	.83	.78	.58	.68	.70	.69

4. Asthma (cont)

TABLE 4c. Use of Medications for Control of Asthma-Persistence

Prescription drug classes included in this table are:

- •Inhaled corticosteroids (Class A)
- •Cromolyn sodium and nedocromil (Class B)
- •Methylxanthines (Class C)
- •Leukotriene modifiers (Class D)
- •Antimuscarinic agents (Class E)
- •Long acting beta-agonists (inhaled and tablet) (Class F)

The values in the table represent the median length of time (in days) a patient went without a drug.

	Median Days Without Drug For Class A Patients	Median Days Without Drug For Class B Patients	Median Days Without Drug For Class C Patients	Median Days Without Drug For Class D Patients	Median Days Without Drug For Class E Patients	Median Days Without Drug For Class F Patients	Median Days Without Drug For Mult Class	Median Days Without Drug For Any Class
AGE								
0-4	39.0	41.4		13.5	34.2	50.0	27.3	29.0
5-9	38.7	32.4		15.4	38.0	32.5	23.5	24.3
10-17	34.0	50.2	14.3	17.3	27.2	30.0	26.0	25.0
18-34	29.5	23.7	7.20	12.2	33.5	23.4	24.0	21.0
35-44	28.8	25.4	13.5	9.50	32.5	24.2	20.8	20.8
45-54	27.0	42.2	12.0	9.00	25.7	22.3	18.0	19.0
55-64	25.0	44.4	8.17	7.00	21.0	20.3	15.5	17.0
65-84	25.1	33.5	6.00	7.74	24.3	20.0	16.4	18.0
85+	24.9		12.4	4.00	22.0	19.5	11.5	13.0
GENDER								
Male	30.5	33.5	8.11	13.0	23.5	25.0	22.0	23.0
Female	29.7	40.2	10.4	10.5	25.9	24.0	19.8	20.2
GEOGRAPHIC AREA								
Urban	30.0	32.1	8.16	11.5	25.1	24.0	20.4	21.3
Rural	31.0	41.3	11.0	12.0	24.7	26.0	22.0	21.5
TOTAL	30.0	37.6	9.33	11.7	25.0	24.3	20.8	21.4

4. Asthma (cont)

TABLE 4d. Use of Rescue/Quick-Relief Medications Among Asthma Patients

Prescription drugs included in this table are:

•Short-acting agonists (inhaled) (Class G)

	% of Patients Receiving At Least One Rescue Med Prescription	Average Number of Rescue Med Prescriptions Per Patient Month
AGE		
0-4	44.3%	0.63
5-9	48.1%	0.53
10-17	53.7%	0.61
18-34	48.4%	0.73
35-44	52.2%	0.66
45-54	49.0%	0.63
55-64	50.3%	0.73
65-84	58.3%	0.81
85+	58.8%	0.81
GENDER		
Male	50.5%	0.67
Female	48.8%	0.66
GEOGRAPHIC AREA		
Urban	50.3%	0.66
Rural	47.3%	0.68
TOTAL	49.5%	0.66

To be included in this table patients had to receive one or more prescriptions for any of Classes A-F from tables 4A-4C (denominator inclusion)
One or more prescriptions for a rescue med (Class G) serves as the numerator inclusion

Asthma - Key Findings

Prevalence:

1) The **overall rate** of patients receiving a medication from one or more of the asthma indicator drug classes is **84 patients per 1000 member years.**

2) This rate is **higher among females** (88 patients per 1000 member years) than males (81 patients per 1000 member years) and is **roughly twice as high among urban patients** (103 patients per 1000 member years) than rural patients (54 per 1000).

3) **40% of patients receive only rescue/quick-relief meds**.

4) 42% of patients receive combination therapy (more than one drug class).

5) Among medications used for long-term control of asthma, **inhaled corticosteroids** are the most common medication type prescribed (37% of patients). 33% of patients receive **long acting beta-agonists**, the next most common class prescribed.

Medication Possession Ratio (MPR):

1) **The Medication Possession Ratio (MPR) for the six long term control classes shows wide variation**, ranging from .56 for cromolyn sodium/necrodomil to .83 for methylxanthines.

2) The two most commonly prescribed long-term control classes – inhaled corticosteroids and long acting beta-agonists – had MPRs of .63 and .68, respectively.

3) **Five of the six classes have Medication Possession Ratios between .20 and .80, indicating partial adherence. Only one class has an MPR above .80, indicating adherence.**

Asthma - Key Findings continued

Persistence:

1) While overall persistence values for the other chronic disease indicators ranged from seven to eleven days, **overall persistence for asthma was highest at 21.4 days.**

2) Persistence values for the six medication classes used for asthma control can be grouped into three pairs:

   Persistence of 9-12 days: Methylxanthines, leukotriene modifiers
   Persistence of 24-25 days: Antimuscarinic agents, long acting beta-agonists
   Persistence of 30-38 days: Inhaled corticosteroids, cromolyn sodium

3) **Persistence values tend to improve with age.**

Use of Rescue/Quick-Relief Medications:

1) Among all patients receiving at least one prescription for a long-term control medication, **50% received one or more rescue medication prescriptions** during the twelve month period.

2) **Patients in the above group (received long-term control medications and at least one rescue medication prescription) averaged 1.33 prescriptions for rescue medications per month**.

Asthma - Limitations

1) In addition to rescue/quick-relief meds (Class G), six classes for long term control of asthma are examined (Classes A-F). **For purposes of this indicator the assumption was made that if patients received a long term control medication they should continue receiving it routinely.** If patients were for some reason only scheduled to take long term control medications on an intermittent or as needed basis, the MPR and persistence values would look worse than actual.

2) **Diagnosis information is not available in these records**. As many of the drugs used to treat asthma are also used to treat other conditions such as chronic obstructive pulmonary disease (COPD), **some patients whose data are analyzed in this indicator will not be receiving these drugs for asthma**.

3) Definite plan entry and exit dates for participants are not known. As such, decision rules used to calculate medication possession ratio and persistence will likely yield:

    - a higher (more favorable) MPR value than is the case
    - a lower (more favorable) persistence value than is the case

Asthma - Discussion

Background

Asthma is one of the most common chronic diseases worldwide and its prevalence has been increasing, especially among children.[1] The prevalence of asthma diagnosis is approximately 7.5% in Utah, and young adults (18-24) and older adults (55-65) reported the highest diagnosed asthma prevalence.[2] In the same year, 50% of Utahns with asthma reported an asthma attack and experienced asthma symptoms one or more times per week, and 38% of those reported not to be controlled on an asthma medication.[2] The cost of asthma has been reported to be as high as $1.2 billion, but the cost of non-compliance to asthma therapy and of not treating with appropriate controller medications is even higher.[3]

Although there is no cure for asthma, many lifestyle and pharmacologic measures can be taken to control asthma. Inhaled glucocorticosteroids, systemic glucocorticosteroids, methylxanthines, long-acting inhaled beta 2- agonists, long-acting oral beta 2- agonists, leukotriene modifiers, anti-IgE, and second generation antihistamines have been used to provide long-term control of asthma. Rapid-acting inhaled beta 2-agonists, systemic glucocorticosteroids, inhaled anticholinergics, short-acting theophylline, and short-acting oral 2-agonists are used as reliever medications in conjunction with the long-term control medications. The aims of these pharmacologic therapies are to prevent or minimize chronic and nocturnal symptoms, minimize exacerbations, prevent emergency room visits, eliminate or minimize the use of as-needed beta 2 –agonist, achieve approximately normal PEF, and ultimately achieve normal daily life including exercise and physical activity while producing no adverse effects from the prescribed medication.[1]

In 1993, the National Heart, Lung, and Blood Institute joined with the World Health Organization to compile the "Global Strategy for Asthma Management and Prevention," which included a management plan for asthma. Several updates have been made to this report by the Global Initiative for Asthma since the 1993 report. The guideline used in this report is based on the latest Global Initiative for Asthma report published on October of 2004.

Rationale for the indicator

This indicator will focus on the use of long-term asthma control medications, compliance in use of long-term control medications (using refill patterns as a proxy), and the use of quick-relief medications. Information could be used for provider education and health plan quality improvement projects. One of the Healthy People 2010 objectives is to increase the proportions of persons with asthma who receive appropriate asthma care according to national guidelines, particularly for those persons who receive medication regimes that prevent the need for more than one canister of short-acting (reliever) medication per month. A pharmacy database also can be used to estimate the prevalence of asthma, track the ratio of the two drugs as indicator of care, and develop interventions to reduce emergency department visits and hospitalizations. The Utah Asthma Control Program proposed this indicator.

Description of the Indicator

This indicator will focus on the use of long-term asthma control medications, compliance in use of long-term control medications (using refill patterns as a proxy), and the use of quick-relief medications. One of the Healthy People 2010 objectives is to increase the proportions of persons with asthma who receive appropriate asthma care according to national guidelines, particularly those persons who receive medication regimes that prevent the need for more than one canister of short-acting (reliever) medication per month.

Uses of the Information

The Utah Department of Health Asthma Program, which proposed this indicator, has facilitated and partnered with the Utah Asthma Task Force to develop a statewide strategic plan to address asthma in Utah. The asthma medication information and report will be presented to the Task Force. The information can be used for health plan quality improvement projects and provider education; for primary and preventive care providers to track the ratio of the two drugs as indicator of care, and develop interventions to reduce emergency department (ED) visits and hospitalizations, and for state and local public health programs to estimate the prevalence and severity of asthma in the population and monitor the trends.

Disease classification and treatment guidelines

The severity of asthma is classified into 4 steps based on the clinical signs and symptoms prior to treatment. The medications used at every step require a reliever medication with or without a controller medication. Details of each asthma step and the medications recommended at each step are described in Table 1. The primary goal of therapy at each step is to treat the underlying disease with controller medication and reduce excess use of short-acting ß-agonists. Over use of short-acting ß-agonists is a well established risk factor for increased mortality.[4, 5] Appropriate treatment of asthma may be realized with an array of different drug combinations, depending on the severity of asthma and the choice of medication. The use of multiple types of medication and the severity of asthma results in different combinations of treatments for patients. Evaluating asthma treatment patterns at the population level will be an important tool for influencing asthma control and appropriate treatment. The guidelines presented below will be used to help interpret the asthma indicator finding.

The Utah Department of Health Asthma Program endorses the National Heart, Lung, and Blood Institute National Asthma Education and Prevention Program's "Guidelines for the Diagnosis and Management of Asthma" found at http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm

Table 1. Recommended asthma medication by asthma severity for adults and children older than 5 years of age*

Level of Severity	Daily Controller Medication	Other Treatment Options†
Step 1‡ • Symptoms less than once a week • Brief exacerbations • Nocturnal symptoms ≤2 times per month • FEV1 or PEF ≥ 80% predicted • FEV1 or PEF variability <20%	• None necessary	
Step 2 • Symptoms more than once a week but less than once a day • Exacerbations may affect activity and sleep • Nocturnal symptoms >2 times per month • FEV1 or PEF ≥ 80% predicted • FEV1 or PEF variability 20-30%	• Low-dose inhaled corticosteroid	• Sustained release theophylline, or • Cromone, or • Leukotriene modifier
Step 3 • Symptoms daily • Exacerbations may affect activity and sleep • Nocturnal symptoms more than once per week • Daily use of inhaled short-acting ß2-agonist • FEV1 or PEF 60-80% predicted • FEV1 or PEF variability >30%	• Low- to medium-dose inhaled corticosteroid plus long-acting ß2-agonist	• Medium dose inhaled glucocorticosteroid plus sustained release theophylline, or • Medium-glucocorticosteroid plus long-acting oral ß2-agonist, or • High-dose inhaled glucocorticosteroid or • Medium-dose inhaled glucocorticosteroid plus leukotriene modifier
Step 4 • Symptoms daily • Frequent exacerbations • Frequent nocturnal asthma symptoms • Limitation of physical activity • FEV1 or PEF ≤60% predicted • FEV1 or PEF variability >30%	• High-dose inhaled corticosteroid plus long-acting ß2-agonist plus one of the following, if needed: 1. Sustained release theophylline 2. Leukotriene modifier 3. Long-acting oral ß2-agonist 4. Oral glucocorticosteroid	

*Adapted from Global Initiative for Asthma Report

†Other treatment options listed in order of increasing cost.

‡ Patients with intermittent asthma but severe exacerbations should be treated as having moderate persistent asthma

Previous studies

Several retrospective studies have examined prescription use among asthmatics. A PubMed search of the terms asthma, prevalence, adherence, compliance, guideline and database were for this review. The evidence table describes prescription claims studies that may be similar or relevant to the current project. This information can be used to compare the Utah findings to other populations.

Evidence Table 1.

<table>
<tr><th>Reference/ Study Design</th><th>N</th><th>Study Objectives</th><th>Methods</th><th>Results</th><th>Grade*</th></tr>
<tr><td>Williams et al[6] 2004</td><td>405</td><td>• To estimate the proportion of poor asthma-related outcomes attributable to ICS non-adherence in a large health maintenance organization in Michigan</td><td>• Days supplied = dividing the canister size by the dosage information
• Adherence
• Continuous, multiple-interval measure of medication availability
• Continuous, multiple-interval measure of medication gaps</td><td>• ~50% overall adherence to ICS
• Adherence significantly and negatively correlates with asthma-related ED visits, number of fills of oral steroids, and number of days of oral steroids use
• Adherences is not significantly correlated with asthma-related outpatient visits and hospitalization</td><td>3</td></tr>
<tr><td>David C[7] 2004

Retrospective, descriptive study</td><td>29,707</td><td>• To determine the changes in prescribing of daily anti-inflammatory drugs for children in Florida Medicaid during the first 2 years after publication of the Guidelines and seven years later</td><td>• Data extraction from outpatient-pharmacy claims records for children obtaining medicine commonly used for asthma
• Daily anti-inflammatory drugs
• Drug classes include: ß-agonists, theophyllines, oral corticosteroids, inhaled corticosteroids, cromolyn and nedocromil, montelukast</td><td>• Percentage of prescriptions for the asthma medication:
<table>
<tr><th>Drug Class</th><th>1990-1992</th><th>1997-1999</th></tr>
<tr><td>ß-agonists</td><td>62.6</td><td>60.3</td></tr>
<tr><td>theophyllines</td><td>16.6</td><td>4.6</td></tr>
<tr><td>oral corticosteroids</td><td>6.9</td><td>9.6</td></tr>
<tr><td>inhaled corticosteroids</td><td>3.9</td><td>13.3</td></tr>
<tr><td>cromolyn and nedocromil</td><td>10</td><td>7.9</td></tr>
<tr><td>montelukast</td><td>-</td><td>4.3</td></tr>
</table></td><td>3</td></tr>
</table>

Lynd D et al[8] 2002 Retrospective cohort analysis	78,758	• To assess trends in asthma management and to identify factors associated with increasing short-acting ß-agonists utilization in British Columbia using administrative prescription data between 1996 and 1998	• Trend analysis of the annual prevalence of not receiving a prescription for an ICS • Analysis of transitions between receiving and not receiving an ICS prescription • Categorization for ß-agonists use • Controlled– Less than 4 canisters in one year • Uncontrolled – Greater than 4 canisters in one year	• Approximately 80% of the patients received ≤4 canisters of ß-agonists and approximately 3% of patients received >20 canisters in one year • Trend analysis demonstrated 14.9% of patients increased and 16.8 % of patients decreased in their usage of ß-agonists during the 3 years • Approximately 40% of the patients in the population did not fill a prescription for an ICS annually	3
Shireman T et al[9] 2002 Retrospective, cross-sectional analysis	10,959	• To find correlation between inappropriate asthma drug therapy patterns and selected patient demographics to healthcare utilization	• Calculated average daily doses of oral and inhaled asthmatic medications • Primary outcome measures included the occurrence and frequency of oral steroid bursts, asthma-related hospitalizations, and asthma-related emergency department visits	• 44.5% of the study population did not receive an ICS • 71% of the study population received ≥1 puff per day of a short-acting ß-agonists (25.4% received 3-7.99 puffs per day, 18.2% received >8 puffs per day), and approximately 20% has no/minimal use of ICS • 23.9% received long-acting ß-agonists, 25.1% received leukotriene modifiers, and 27% received theophylline • Patients on high doses of short-acting ß-agonists had the greatest odds of receiving an oral steroid bursts and be hospitalized • Patients on high doses of short-acting ß-agonists and high doses of ICS were twice as likely to have an ED visit • The use of short-acting ß-agonists is highly significant and positively correlated with ED visits	3

Piecoro LT et al 2001 Retrospective, descriptive analysis	24,365	• Cost of asthma in Medicaid program • To determine if patients are receiving appropriate therapy • To assess if nonadherence to guideline is associated with increased asthma-related ER care and hospitalization	• Asthma patients were identified using a medical claimin Kentucky Medicaid administrative data for 1996 • Daily or overuse of inhaled short-acting ß-agonists (greater than 1 canister per month) in the absence of concurrent ICS was considered to be nonadherence to the guideline	• Asthma prevalence is highest among AA and this group also had higher rates of office visits, ED, and hospitalization compared to whites • <10% of daily users of short-acting ß-agonists used ICS • Daily use of short-acting ß-agonists was associated with higher rates of hospitalization (OR=1.5, p<.05) • AA (OR=1.6) and prescription for oral steroids (OR=1.3) were significantly associated with higher asthma-related hospitalization	3
Berger WE et al 2004	49,637	• To evaluate the HEDIS measure of appropriate use of asthma medications	• Controller group included patients using ICS, mast cell stabilizaers, leukotriene inhibitors, or methylxanthines only	• ~35.7% were using 1 class of long-term controller medications, 18.4% were using more than 1 class, and 45.9% were not using such medication • Patients with low adherence to controller medication had a significantly higher risk of visit and hospitalization relative to non users • Patients receiving ICS had the lowest risk of ED visit or hospitalization (OR=.37)	3

Abbreviations: AA=African Americans; ED = emergency department; HEDIS =Health Plan Employer Data and Information Set; ICS = inhaled corticosteroids; OR=odds ratio

* Grade of Scientific Evidence. Refer to end of document for definitions.

References

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Indicator 5 – Adolescent Depression

Adolescent Depression - Introduction

Depression among adolescents and children has been a topic that has received increasing attention in recent years. Overall antidepressant use by children and adolescents, as reported by numerous studies, is on the rise.

Concerns over safety of antidepressant use in children and adolescents have also been noted. Only one antidepressant, Prozac, is approved by the FDA for use in children. Specific warnings stating that Paxil and Effexor should not be used in children were issued in 2003. This was followed by the October 2004 FDA public health advisory directing manufacturers of all antidepressants to include a "black box" warning of increased risk of suicidal thoughts and behavior when antidepressants are used in adolescents and children.

This indicator focuses on antidepressant use in the 0-4, 5-9, and 10-18 age groups. Values for adult age groups are also listed for comparative purposes.

5. Adolescent Depression

TABLE 5a. Use of Medications for Control of Depression-Prevalence

Prescription drug classes included in this table are:

- •amitriptyline (Elavil), buproprion (Wellbutrin), citalopram (Celexa), fluoxetine (Prozac), fluvoxamine (Luvox), mirtazapine (Remeron) nefazodone (Serzone), sertraline (Zoloft), trazodone (Desyrel) (Class A)
- •venflafaxine (Effexor) (Class E)
- •paroxetine (Paxil) (Class P)

	# of Class A Patients	# of Class E Patients	# of Class P Patients	# of Mult Class Patients	Total # of Patients on Any Class	# of Patients Per 1,000 Member Years
AGE						
0-4	354	10	42	14	392	3
5-9	2,888	58	399	162	3,179	32
10-17	12,521	1,022	1,959	1,106	14,364	102
18-34	39,415	5,494	6,930	4,127	47,531	204
35-44	26,534	3,824	4,165	2,991	31,429	305
45-54	25,281	3,400	3,751	2,748	29,591	319
55-64	13,263	1,602	2,161	1,426	15,555	299
65-84	5,340	436	962	534	6,188	319
85+	1,102	56	233	96	1,294	471
GENDER						
Male	39,650	4,702	7,146	3,729	47,631	114
Female	87,048	11,200	13,456	9,475	101,892	230
GEOGRAPHIC AREA						
Urban	97,626	12,549	15,248	10,171	114,895	217
Rural	29,072	3,353	5,354	3,033	34,628	104
TOTAL	126,698	15,902	20,602	13,204	149,523	174

Depression statistics for adult age categories are listed for comparative purposes

5. Adolescent Depression (cont)

TABLE 5b. Use of Medications for Control of Adolescent -Medication Possession Ratio (MPR)

Prescription drug classes included in this table are:

- •amitriptyline (Elavil), buproprion (Wellbutrin), citalopram (Celexa), fluoxetine (Prozac), fluvoxamine (Luvox), mirtazapine (Remeron) nefazodone (Serzone), sertraline (Zoloft), trazodone (Desyrel) (Class A)
- •venflafaxine (Effexor) (Class E)
- •paroxetine (Paxil) (Class P)

MPR greater than .80 Adherent
MPR from .20 to .80 Partially adherent
MPR less than .20 Nonadherent

	MPR of Class A Patients	MPR of Class E Patients	MPR of Class P Patients	MPR of Patients on Mult Class	MPR of Patients on Any Class
AGE					
0-4	.80	.83	.87	.83	.81
5-9	.79	.81	.84	.79	.79
10-17	.78	.84	.80	.76	.78
18-34	.78	.84	.80	.75	.78
35-44	.79	.84	.81	.80	.80
45-54	.81	.85	.82	.82	.82
55-64	.83	.86	.83	.84	.83
65-84	.85	.87	.86	.86	.85
85+	.87	.87	.88	.86	.87
GENDER					
Male	.80	.86	.82	.80	.81
Female	.80	.84	.81	.79	.80
GEOGRAPHIC AREA					
Urban	.80	.85	.82	.80	.81
Rural	.80	.84	.81	.78	.80
TOTAL	.80	.85	.82	.79	.80

Depression statistics for adult age categories are listed for comparative purposes

5. Adolescent Depression (cont)

TABLE 5c. Use of Medications for Control of Depression-Persistence

Prescription drug classes included in this table are:

- •amitriptyline (Elavil), buproprion (Wellbutrin), citalopram (Celexa), fluoxetine (Prozac), fluvoxamine (Luvox), mirtazapine (Remeron) nefazodone (Serzone), sertraline (Zoloft), trazodone (Desyrel) (Class A)
- •venflafaxine (Effexor) (Class E)
- •paroxetine (Paxil) (Class P)

The values in the table represent the median length of time (in days) a patient went without a drug.

	Median Days Without Drug For Class A Patients	Median Days Without Drug For Class E Patients	Median Days Without Drug For Class P Patients	Median Days Without Drug For Mult Class	Median Days Without Drug For Any Class
AGE					
0-4	11.7	47.0	4.00	13.0	10.7
5-9	11.0	9.00	8.59	11.0	10.7
10-17	12.4	9.00	11.0	14.0	12.0
18-34	12.0	7.67	9.75	13.8	11.5
35-44	11.0	7.50	9.50	12.0	10.5
45-54	10.0	7.00	8.67	10.0	9.33
55-64	9.50	7.00	9.00	10.5	9.00
65-84	9.00	7.00	8.10	10.0	8.80
85+	7.50	8.68	7.00	9.20	7.33
GENDER					
Male	10.5	7.00	9.00	12.0	10.0
Female	11.0	7.75	9.50	12.0	10.7
GEOGRAPHIC AREA					
Urban	11.0	7.38	9.17	11.9	10.3
Rural	11.1	8.00	9.60	12.7	10.8
TOTAL	11.0	7.50	9.33	12.0	10.5

Depression statistics for adult age categories are listed for comparative purposes

Adolescent Depression - Key Findings

Prevalence:

1) The **overall rate** of patients aged 10-17 receiving a medication from one or more of the adolescent depression drug classes is **102 patients per 1000 member years.** This figure is lower than the rate of 262 per 1000 patients seen in adults 18 and over.

2) This rate among children aged 0-4 was 3 patients per 1000 member years and was 32 patients per 1000 member years among children aged 5-9.

3) **21% of patients aged 10-17 receiving a medication from one or more of the adolescent depression drug classes received Effexor or Paxil**.

4) For all age groups, rate of patients receiving a medication from one or more of these drug classes **was more than twice as high among female patients** (230 patients per 1000 member years) than male patients (114 patients per 1000 member years). **The rate was also more than twice as high among urban patients** (217 patients per 1000 member years) than rural patients (104 patients per 1000 member years).

Medication Possession Ratio (MPR):

1) The Medication Possession Ratio (MPR) for patients aged 10-17 (as well as the two younger age groups) is similar to the overall MPR.

Persistence:

1) The median length of time patients went without their medication tends to decrease (improve) with increasing age. There are not significant differences by gender or patient location (urban/rural).

Adolescent Depression - Limitations

1) **These analyses are based on 2003 data**. As the FDA announcement that Paxil should not be prescribed for children under 18 years of age due to an increased risk of suicide/self-harm was issued in **June 2003**, and the drug manufacturer letter to doctors warning that Effexor should not be prescribed to children due to similar safety concerns was issued in **August 2003**, **many of the patients receiving Effexor or Paxil in these data received the prescription prior to the June FDA warning on Paxil/August manufacturer letter on Effexor**.

2) **Diagnosis information is not available in these records.** As more of the drugs in this indicator are actually approved for OCD than depression, not all patients in this indicator will be receiving medication for depression.

3) Definite plan entry and exit dates for participants are not known. As such, decision rules used to calculate medication possession ratio and persistence will likely yield:

    - a higher (more favorable) MPR value than is the case
    - a lower (more favorable) persistence value than is the case

Adolescent Depression - Discussion

Background

Depression among adolescents and its treatment has recently been the center of much debate. A January 2003 article in *Archives of Pediatrics and Adolescent Medicine* reported that the number of psychotropic medication prescribed to children and adolescents more than doubled from 1987 to 1996.[1] Of the 900,000 youths examined, antidepressants ranked second in terms of type of psychotropic medication prescribed. The authors concluded that "Youth psychotropic treatment utilization during the 1990s nearly reached adult utilization rates". This pattern holds true even for younger children; the number of two to four year olds on psychiatric medication increased 50% between 1991 and 1995.[2] In addition, this study found that "decreases occurred in the relative proportions of previously dominant psychotherapeutic agents in the stimulant and antidepressant classes, while increases occurred for newer, less established agents". A more recent study evaluated the prevalence of prescription antidepressant use among children and adolescents with nationwide data from 1998 to 2002.[3] The researchers found the overall prevalence of antidepressant use among children increased from 1.6% to 2.4% in 2002. The adjusted annual increase was 9.2%. The trend of increasing overall use of antidepressants among children and adolescents was driven primarily by greater use of selective serotonin reuptake inhibitors.

Many antidepressants that have undergone rigorous clinical trials for adults have not been studied as thoroughly in children. As such, most antidepressants for children are prescribed "off-label" – while the medication has received FDA approval for treatment of a specific disease in adults, it has not received official approval for treatment of the same disease in children. In June 2001 the FDA announced that Paxil® should not be prescribed for children under 18 years of age due to an increased risk of

suicide/self-harm. In August of 2003, drug manufacturers wrote in a letter to doctors that Effexor® should not be prescribed for children for the same reason.

In October, 2004 the FDA issued a public health advisory to warn of the increased risk of suicidality associated with use of antidepressants in children and adolescents. The FDA has directed manufacturers to revise the safety labeling of all antidepressant drugs to include "black box" and expanded warnings of the increased risk of suicidality and updated results from pediatric studies. The FDA has also informed antidepressant manufacturers that a MedGuide is to be dispensed with the medication to advise patients and their caregivers of the risk and precautions that may be taken.

Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. There has been a long-standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients. A causal role for antidepressants in inducing suicidality has been established in pediatric patients.

Pooled analyses of short-term placebo-controlled trials of nine antidepressant drugs (SSRIs and others) in children and adolescents with major depressive disorder (MDD), obsessive compulsive disorder (OCD), or other psychiatric disorders (a total of 24 trials involving over 4,400 patients) have revealed a greater risk of adverse events representing suicidal behavior or thinking during the first few months of treatment in those receiving antidepressants. The average risk of such events on drug was 4%, twice the placebo risk of 2%. There was considerable variation in risk among drugs, but there was a tendency toward an increase for almost all drugs studied. The risk of suicidality was most consistently observed in the MDD trials, but there were signals of risk arising from trials in other psychiatric indications (obsessive compulsive disorder and social anxiety disorder) as well. No suicides occurred in these trials. It is unknown whether

the suicidality risk in pediatric patients extends to longer-term use, i.e., beyond several months. It is also unknown whether the suicidality risk extends to adults.

The FDA advises that the risk of increased suicidality be considered with respect to clinical need before initiating antidepressant therapy in children and adolescents with MDD and other psychiatric disorders, and that prescriptions be written for the lowest possible quantity of tablets to reduce the risk of overdose. Families and caregivers should closely observe pediatric patients being treated with antidepressants for signs of clinical worsening, suicidality, agitation, irritability, and unusual changes in behavior, especially during the first few months after initiation of therapy and upon dosing changes. Daily monitoring and close contact with the prescribing physician are advised.

Pharmacological Treatment

The new antidepressant labeling includes a statement regarding its approved pediatric indication(s). Of the antidepressants, only fluoxetine (Prozac) is approved for use in treating MDD in pediatric patients. Fluoxetine, sertraline (Zoloft), fluvoxamine (Luvox), and clomipramene (Anafranil) are approved for OCD in pediatric patients. None of the drugs is approved for other psychiatric indications in children. The FDA notes that these label warnings apply to the entire category of antidepressants due to a lack of available data to exclude any given drug from the associated increased risk of suicidality.

National statistics

A study by Express Scripts Inc (ESI) is the most recent study to evaluate trends in the use of antidepressants in a national sample with 1.9 million years of commercially insured pediatric patients.[3] From 1998 to 2002, the overall prevalence of antidepressant use increased by 49% (table 1). The overall prevalence of antidepressant use increased at an adjusted rate of 9.2% per year over the study period. The largest year-to-year proportional increase in overall prevalence occurred between 2001 to 2002 (16%). Prevalence increased more for girls (68%) than boys (34%). The overall prevalence of use for all antidepressant classes increased except for tricyclics, which decreased by 29%. Trending for MAOIs was not done due to the small number of prescriptions for this class of antidepressants. SSRIs accounted for the largest increase in antidepressant use (table 2).

Table 1. Prevalence of use of antidepressants in a national random sample of commercially insured children and adolescents stratified by age and gender (replicated from Delate et al, 2004)[3]

Age & Gender	1998 % (SE)	1999 % (SE)	2000 % (SE)	2001 % (SE)	2002 % (SE)	Absolute % Change
Overall sample	1.59 (.02)	1.81 (.02)	1.86 (.02)	2.05 (.02)	2.37 (.02)	0.78
Girls	1.45 (.03)	1.66 (.03)	1.83 (.03)	2.09 (.03)	2.44 (.03)	0.99
Boys	1.73 (.03)	1.95 (.03)	1.90 (.03)	2.02 (.03)	2.31 (.03)	0.58
0-5 years olds						
Girls	0.08 (.01)	0.12 (.02)	0.12 (.02)	0.16 (.02)	0.16 (.02)	0.08
Boys	0.14 (.02)	0.13 (.02)	0.14 (.02)	0.19 (.02)	0.23 (.02)	0.09
6-10 year olds						
Girls	0.57 (.03)	0.64 (.04)	0.72 (.04)	0.7 (.04)	0.84 (.04)	0.27
Boys	1.21 (.05)	1.39 (.05)	1.18 (.05)	1.33 (.05)	1.6 (.05)	0.39
11-14 year olds						
Girls	1.44 (.06)	1.60 (.06)	1.63 (.06)	1.80 (.06)	2.36 (.07)	0.92
Boys	2.56 (.07)	2.77 (.08)	2.64 (.08)	2.85 (.07)	3.12 (.08)	0.56
15-18 year olds						
Girls	3.74 (.09)	4.28 (.1)	4.73 (.11)	5.27 (.1)	6.36 (.11)	2.62
Boys	3. (.08)	3.40 (.08)	3.49 (.08)	3.82 (.08)	4.23 (.09)	1.23

Table 2. Use of subclasses of antidepressants and of paroxetine in a national random sample of commercially insured children and adolescents stratified by gender (replicated from Delate et al, 2004)[3]

Medication and Gender	1998 % (SE)	1999 % (SE)	2000 % (SE)	2001 % (SE)	2002 % (SE)
SSRI					
Girls and boys	0.93 (.02)	1.1 (.02)	1.2 (.02)	1.38 (.02)	1.66 (.02)
Girls	0.93 (.02)	1.14 (.02)	1.27 (.03)	1.48 (.03)	1.83 (.03)
Boys	0.93 (.02)	1.07 (.02)	1.13 (.03)	1.29 (.03)	1.48 (.03)
Paroxetine					
Girls and boys	0.24 (.01)	0.29 (.01)	0.34 (.01)	0.38 (.01)	0.48 (.01)
Girls	0.24 (.01)	0.3 (.01)	0.37 (.02)	0.4 (.01)	0.51 (.02)
Boys	0.23 (.01)	0.28 (.01)	0.32 (.01)	0.36 (.01)	0.44 (.02)
Tricyclics					
Girls and boys	0.48 (.01)	0.46 (.01)	0.42 (.01)	0.34 (.01)	0.34 (.01)
Girls	0.39 (.01)	0.38 (.01)	0.39 (.02)	0.32 (.01)	0.34 (.01)
Boys	0.57 (.02)	0.54 (.02)	0.44 (.02)	0.37 (.01)	0.34 (.01)
Modified cyclics					
Girls and boys	0.12 (.01)	0.14 (.01)	0.15 (.01)	0.15 (.01)	0.16 (.01)
Girls	0.14 (.01)	0.14 (.01)	0.16 (.01)	0.17 (.01)	0.19 (.01)
Boys	0.1 (.01)	0.14 (.01)	0.13 (.01)	0.13 (.01)	0.14 (.01)
Tetracyclics					
Girls and boys	0.02 (0)	0.05 (0)	0.05 (0)	0.08 (0)	0.08 (0)
Girls	0.01 (0)	0.04 (0)	0.04 (0)	0.06 (0)	0.06 (0)
Boys	0.02 (0)	0.06 (.01)	0.06 (.01)	0.09 (.01)	0.11 (.01)
Miscellaneous	0.37 (.01)	0.48 (.02)	0.45 (.02)	0.52 (.02)	0.58 (.02)

Adherence

A retrospective 12-month analysis (1997-1998)was conducted of claims data for a cohort of nine- to 18-year-old new users of antidepressants in an Ohio Medicaid population.[7] The purpose of their study was to identify patterns of new antidepressant use among children and adolescents and to determine whether the duration of treatment was sufficient. They followed a total of 554 children and adolescents who started antidepressant therapy during a three-month period. These children were mostly Caucasians (78 percent), and their average age was 13 years. Boys and girls were equally represented. The use of antidepressants increased with age among girls, but declined among boys. The distribution of antidepressants dispensed was selective serotonin reuptake inhibitors, 47 %; tricyclic antidepressants, 27 %; and other antidepressants, 23 %. The proportion of children who completed treatment was 94 % for the four-week treatment period, 23.5 % for the six-month period, and 12.6 % for the whole year. The authors concluded that, as with adults, continuation of treatment among children and adolescents declines dramatically after an initial period. In addition to studies of the clinical efficacy of antidepressant use among children and adolescents, future research is needed to assess adherence to practice guidelines and health outcomes in childhood and adolescent mental health.

Application

Antidepressant use is of particular interest in Utah because a study released by Express Scripts reported that Utah had the highest rate of antidepressant use in the U.S., even after adjustment for age and gender.[4] Sixteen percent of the Utah population was reported to be receiving antidepressant medication.

This indicator will examine antidepressant prescriptions dispensed for different age groups. The denominators for the utilization rates are the aggregated membership information reported by participating health plans. The analysis will emphasize children/adolescents' uses in comparison with the adult utilization patterns and inappropriate uses (e.g. Paxil® or Effexor® prescribed for children under 18 years of age). The indicator will provide information on the prevalence of various types of antidepressant prescriptions issued to children/adolescents in Utah along with trends in prescribing patterns.

The program will use the information to obtain a baseline of antidepressant use and monitor over- or under-uses of antidepressants and educate providers. If Utah was found to have an unusually high utilization rate over time or use of questionable antidepressant medications among adolescents, the public programs will use this information in dialogues with community organizations (e.g. the Utah Pediatric Partnership to Improve Healthcare Quality) to determine the type and extent of needed intervention to address the use of the medication and the mental health problems among the adolescent population that necessitated the prescriptions.

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Indicator 6 – Depression, OCD and Anxiety Disorders in Pregnancy

Depression, OCD and Anxiety Disorders in Pregnancy - Introduction

Pregnancy presents unique challenges, both physical and emotional, for the expectant mother. The Pregnancy Risk Assessment Monitoring System (PRAMS) study showed that 24% of Utah women who had a live birth in 2000 reported being moderately or very depressed in the postpartum period. In addition to depression, pregnancy can also exacerbate existing (or serve as a trigger for new) obsessive-compulsive tendencies and feelings of anxiety.

This indicator examines use of four medication classes used to treat depression, obsessive-compulsive disorder, and anxiety disorders:

- Selective Serotonin Reuptake Inhibitors (SSRIs)
- Tricyclic Antidepressants (TCAs)
- Newer antidepressants
- Benzodiazepines

6. Depression, OCD and Anxiety Disorders During Pregnancy

TABLE 6a. Use of Medications for Control of Depression, OCD and Anxiety Disorders During Pregnancy- Prevalence

Prescription drug classes included in this table are:

- •SSRIs (Class A)
- •TCAs (Class B)
- •New antidepressants including buproprion (Wellbutrin), nefazodone (Serzone), trazodone (Desyrel), venlafaxine (Effexor), and mirtazapine (Remeron) (Class C)
- •Benzodiazepines (Class D)

	# of Class A Patients	# of Class B Patients	# of Class C Patients	# of Class D Patients	# of Mult Class Patients	Total # of Patients on Any Class	Number of Patients Per 1,000 Member Years
AGE							
10-17	169	14	46	28	42	207	163
18-34	3,151	186	946	720	784	4,050	165
35-44	499	69	237	212	233	729	275
GEOGRAPHIC AREA							
Urban	2,832	197	945	732	802	3,721	170
Rural	987	72	284	228	257	1,265	190
TOTAL	3,819	269	1,229	960	1,059	4,986	175

**The population for this indicator is based on women ages 10 to 44 who are on a pre-natal vitamin. Based on the health plans that submitted data, the number of women ages 10 to 44 on pre-natal vitamins is 28524.

6. Depression, OCD and Anxiety Disorders During Pregnancy (cont)

TABLE 6b. Use of Medications for Control of Depression, OCD and Anxiety Disorders During Pregnancy- Medication Possession Ratio (MPR)

Prescription drug classes included in this table are:

- •SSRIs (Class A)
- •TCAs (Class B)
- •New antidepressants including buproprion (Wellbutrin), nefazodone (Serzone), trazodone (Desyrel), venlafaxine (Effexor), and mirtazapine (Remeron) (Class C)
- •Benzodiazepines (Class D)

MPR greater than .80 **Adherent**
MPR from .20 to .80 **Partially adherent**
MPR less than .20 **Nonadherent**

	MPR of Class A Patients	MPR of Class B Patients	MPR of Class C Patients	MPR of Class D Patients	MPR of Patients on Mult Class	MPR of Patients on Any Class
AGE						
10-17	.72	.74	.73	.40	.68	.71
18-34	.78	.77	.77	.62	.72	.76
35-44	.81	.77	.78	.67	.80	.80
GEOGRAPHIC AREA						
Urban	.79	.78	.77	.63	.75	.77
Rural	.77	.73	.78	.62	.72	.75
TOTAL	.78	.77	.77	.63	.74	.77

6. Depression, OCD and Anxiety Disorders During Pregnancy (cont)

TABLE 6c. Use of Medications for Control of Depression, OCD and Anxiety Disorders During Pregnancy-Persistence

Prescription drug classes included in this table are:

- •SSRIs (Class A)
- •TCAs (Class B)
- •New antidepressants including buproprion (Wellbutrin), nefazodone (Serzone), trazodone (Desyrel), venlafaxine (Effexor), and mirtazapine (Remeron) (Class C)
- •Benzodiazepines (Class D)

The values in the table represent the median length of time (in days) a patient went without a drug.

	Median Days Without Drug For Class A Patients	Median Days Without Drug For Class B Patients	Median Days Without Drug For Class C Patients	Median Days Without Drug For Class D Patients	Median Days Without Drug For Mult Class	Median Days Without Drug For Any Class
AGE						
10-17	15.2	9.75	14.0	34.0	20.8	15.3
18-34	10.4	18.4	11.5	22.0	14.5	11.5
35-44	10.0	16.0	11.3	17.0	11.6	10.9
GEOGRAPHIC AREA						
Urban	10.5	18.5	11.6	20.0	13.2	11.3
Rural	10.8	16.8	11.8	20.4	14.6	12.0
TOTAL	10.5	17.3	11.7	20.0	13.7	11.5

Depression, OCD and Anxiety Disorders in Pregnancy - Key Findings

Prevalence:

1) The **overall rate** of patients receiving a medication from one or more of the drug classes in this indicator is **18 patients per 1000 member years.**

2) **Selective Serotonin Reuptake Inhibitors (SSRIs)** -- including fluoxetine (Prozac), paroxetine (Paxil), and venlafaxine (Effexor) – **were the most commonly prescribed class**, with 77% of patients in this indicator receiving a drug from this class.

3) 21% of patients receive combination therapy (more than one drug class).

Medication Possession Ratio (MPR):

1) The Medication Possession Ratio (MPR) for the three antidepressant classes are remarkably consistent, ranging from .77 to .78.

2) The MPR for benzodiazepines, at .63, is lower than the antidepressant classes. See Limitations for additional information.

3) **The MPR tends to increase (improve) with age**, with the MPR for ages 10-17 at .71, ages 18-34 at .76, and 35-44 at .80.

4) For the three individual antidepressant classes and the benzodiazepine class, only females aged 35-44 taking SSRIs have an MPR (.81) that meets or exceeds the adherence target of .80. For each class, all other age group MPR values (and all urban/rural MPR values) are below .80.

Persistence:

1) The median length of time patients went without SSRIs or newer antidepressants was between ten and twelve days. Tricyclic antidepressants had a higher persistence, at 17.3 days.

Depression, OCD and Anxiety Disorders in Pregnancy - Limitations

1) **Diagnosis information is not available in these records**. As diagnosis of pregnancy cannot be used to select patients, **prenatal vitamins were used as a proxy for pregnancy**. Women between ages 10 and 44 receiving prenatal vitamins were used as the total population (denominator) for this indicator.

   There are obviously limitations in using this approach. According to a March of Dimes survey, 31% of non-pregnant women nationwide reported taking prenatal vitamins in 2002 (examples include women planning to become pregnant and nursing mothers). Also, not all pregnant women will necessarily take prenatal vitamins. As these and other limitations could confound the result up or down, it was unclear whether using prenatal vitamins as a proxy would over- or underestimate the target population of pregnant plan members.

   Using prenatal vitamins as a proxy yields 27256 female patients between the ages of 10 and 44. Extrapolating from this figure to the statewide population yields an estimate on the high end of 81395 female patients between the ages of 10 and 44 taking prenatal vitamins. The actual number of total female patients in Utah between the ages of 10 and 44 taking prenatal vitamins likely lies somewhere in-between (the average of the two figures is 54326 patients).

   The number of births in Utah during calendar year 2003 was **49834.** While the characteristics of the population selected by virtue of taking prenatal vitamins may differ somewhat from the population of pregnant patients, at least in terms of magnitude using prenatal vitamins as a proxy works well.

2) Benzodiazepines are often prescribed to be taken on an as needed basis. **As days supplied and days until next refill are the only data available to calculate MPR/persistence, MPR and persistence are of questionable value for this drug class.**

3) Definite plan entry and exit dates for participants are not known. As such, decision rules used to calculate medication possession ratio and persistence will likely yield:

   - a higher (more favorable) MPR value than is the case
   - a lower (more favorable) persistence value than is the case

Depression, OCD and Anxiety Disorders in Pregnancy - Discussion

Background

Depression carries a negative stigma at the work environment as a result of employer and patient attitudes, legal and policy frameworks.[1] This has been associated with loss of employment opportunities because of bias in the workplace.[1] An estimated 4% to 17.6% of all women of childbearing age suffer from depression.[2, 3] The Pregnancy Risk Assessment Monitoring System (PRAMS) study showed that 24% of Utah women who had a live birth in 2000 reported being moderately or very depressed in the postpartum period. Similarly to a potential employee for an organization, expectant mothers may not fully explore all treatment options in fear of losing their children.[4] Depression may be more common in expectant mothers with larger family burden such as other children to take care of or more social responsibilities. Untreated maternal depression have been associated with negative pregnancy outcomes and excess child resource services.[5, 6] Thus, there is a clinical demand for antidepressant use during pregnancy.

Treatment of depression during pregnancy should balance optimal antidepressant use while protecting the welfare of the child. The thalidomide disaster in the 1960s raised many concerns of drug safety during pregnancy, and the Food and Drug Administration developed a standardized rating scale for evaluating the safety of these drugs during pregnancy. All of the drugs contain a FDA category of C which indicates, "either studies in animals have revealed adverse effects on the fetus and there are no controlled studies in women, OR studies in women and animals are not available." Despite such classification, antidepressants are widely used in pregnant women.

The indicator will aim to provide information on the prevalence of prescriptions for antidepressants, obsessive compulsive disorder medications, and anxiolytic

medications issued to pregnant women in Utah along with trends in prescribing patterns. This will provide information to target interventions to proper antidepressant use.

However, as diagnosis data is not available in the pharmacy data it is not possible to determine which female patients are pregnant through this means. One possible solution is employ use of prenatal vitamins as a proxy. This will be an imprecise determinant. According to a March of Dimes survey, 31% of non-pregnant women nationwide reported taking prenatal vitamins in 2002. Also, not all pregnant women are likely to take prenatal vitamins. This figure, will be compared to the number of live births per year in Utah for the same time period to gauge its accuracy. Tracking depression in pregnancy will enable the program to compare the estimated number of women reporting depression via the Pregnancy Risk Assessment Monitoring Survey (PRAMS) with those receiving appropriate treatment.

Uses of the Information

The Utah Reproductive Health Program proposed this indicator. This new indicator will expand depression monitoring to pregnant women from the PRAMS study. Data will be analyzed and reported in aggregate form and will not be published by individual health plan. The first-year data will provide a baseline for the program to assess potential problems of depression among pregnant women in Utah. The intent is to track trends over time and to identify geographic areas of the state that appear to have pockets of need in order to target public and provider educational interventions to appropriate use of depression medication for pregnant women.

The Reproductive Health Program conducts educational intervention through Internet and mailings. The educational intervention-information developed from the Depression in Pregnancy Indicator analysis can be published in the program's pregnancy educational materials and mailed to more than 700 obstetricians, family practitioners, and certified nurse midwives in Utah, and posted on the Internet to facilitate access to this information.

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Indicator 7 - Antipsychotics

Use of Antipsychotics - Introduction

Antipsychotics are medications most commonly associated with use for treatment of schizophrenia. Antipsychotics can be divided into two main groups – typical psychotics and atypical antipsychotics.

Typical antipsychotics are the older class of antipsychotic medications. Atypicals are the newer class and are typically associated with fewer side effects. Atypical antipsychotics can also be effective in patients who fail to respond to typical antipsychotics. However, atypical antipsychotics are among the most costly of all medications, resulting in scrutiny of their use and especially polypharmacy (use of more than one of these medications).

This indicator focuses on use of the two major classes of antipsychotics:

- Typical antipsychotics
- Atypical antipsychotics

7. Use of Antipsychotics

TABLE 7a. Use of Antipsychotic Medications-Prevalence

Prescription drug classes included in this table are:

- •Atypical antipsychotics: including clozapine (Clozaril), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon) (Class A)
- •Typical antipsychotics: including haloperidol (Haldol), chlorpromazine (Thorazine), fluphenazine (Prolixin) (Class T)

	# of Class A Patients	# of Class T Patients	# of Mult Class Patients	Total # of Patients on Any Class	# of Patients Per 1,000 Member Years
AGE					
0-4	90	7	3	94	1
5-9	787	38	14	811	8
10-17	2,585	73	41	2,617	19
18-34	4,352	401	264	4,489	19
35-44	3,073	495	301	3,267	32
45-54	2,673	494	275	2,892	31
55-64	1,382	254	117	1,519	29
65-84	1,436	245	121	1,560	80
85+	524	59	25	558	203
GENDER					
Male	8,064	1,072	620	8,516	20
Female	8,838	994	541	9,291	21
GEOGRAPHIC AREA					
Urban	13,200	1,592	885	13,907	26
Rural	3,702	474	276	3,900	12
TOTAL	16,902	2,066	1,161	17,807	21

7. Use of Antipsychotics (cont)

TABLE 7b. Use of Antipsychotic Medications-Medication Possession Ratio (MPR)

Prescription drug classes included in this table are:

- Atypical antipsychotics: including clozapine (Clozaril), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon) (Class A)
- Typical antipsychotics: including haloperidol (Haldol), chlorpromazine (Thorazine), fluphenazine (Prolixin) (Class T)

MPR greater than .80 Adherent
MPR from .20 to .80 Partially adherent
MPR less than .20 Nonadherent

	MPR of Class A Patients	MPR of Class T Patients	MPR of Patients on Mult Class	MPR of Patients on Any Class
AGE				
0-4	.79	.75	.73	.79
5-9	.80	.70	.73	.80
10-17	.82	.78	.83	.82
18-34	.81	.75	.83	.81
35-44	.83	.71	.85	.82
45-54	.85	.74	.87	.84
55-64	.85	.76	.88	.85
65-84	.87	.73	.83	.86
85+	.86	.76	.76	.85
GENDER				
Male	.84	.72	.84	.83
Female	.83	.76	.85	.83
GEOGRAPHIC AREA				
Urban	.83	.74	.84	.83
Rural	.83	.74	.86	.83
TOTAL	.83	.74	.85	.83

7. Use of Antipsychotics (cont)

TABLE 7c. Use of Antipsychotic Medications-Persistence

Prescription drug classes included in this table are:

- •Atypical antipsychotics: including clozapine (Clozaril), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon) (Class A)
- •Typical antipsychotics: including haloperidol (Haldol), chlorpromazine (Thorazine), fluphenazine (Prolixin) (Class T)

The values in the table represent the median length of time (in days) a patient went without a drug.

	Median Days Without Drug For Class A Patients	Median Days Without Drug For Class T Patients	Median Days Without Drug For Mult Class	Median Days Without Drug For Any Class
AGE				
0-4	13.0	10.0	20.7	12.3
5-9	10.0	19.0	12.1	10.3
10-17	9.91	12.6	8.89	10.0
18-34	10.9	12.0	9.62	10.9
35-44	10.0	15.0	9.80	10.3
45-54	9.00	14.0	8.00	9.20
55-64	8.67	11.0	8.00	8.67
65-84	8.00	12.6	8.25	8.00
85+	8.86	13.0	13.0	9.00
GENDER				
Male	9.50	14.3	9.20	9.75
Female	9.75	12.5	9.00	9.80
GEOGRAPHIC AREA				
Urban	9.75	13.5	9.36	10.0
Rural	9.25	13.3	8.00	9.33
TOTAL	9.67	13.5	9.00	9.75

Use of Antipsychotics - Key Findings

Prevalence:

1) The **overall rate** of patients receiving a medication from one or more of the antipsychotic indicator drug classes is **21 patients per 1000 member years.**

2) This rate is **higher among patients aged 65 to 84** (80 patients per 1000 member years) and **aged 85 and over** (203 patients per 1000 member years).

3) The rate of antipsychotic use was roughly the same in males and females.

4) This rate is **higher among urban patients** (26 patients per 1000 member years) than rural patients (12 patients per 1000 member years).

5) **95% of patients on antipsychotics are on an atypical antipsychotic**.

Medication Possession Ratio (MPR):

1) The Medication Possession Ratio (MPR) for **atypical antipsychotics** (.83) is **higher (better) than that of typical antipsychotics** (.74).

2) MPR is similar for male/female patients and urban/rural patients.

Persistence:

1) The median length of time patients went without their antipsychotic drug was **higher (worse) for typical antipsychotics** (13.5 days) than atypical antipsychotics (9.7 days).

2) Persistence was roughly the same for males and females.

Use of Antipsychotics - Limitations

1) Diagnosis information is not available in these records. This precludes the possibility of examining antipsychotic prescribing patterns for various conditions.

2) Definite plan entry and exit dates for participants are not known. As such, decision rules used to calculate medication possession ratio and persistence will likely yield:

    - a higher (more favorable) MPR value than is the case
    - a lower (more favorable) persistence value than is the case

Use of Antipsychotics - Discussion

Background

The first atypical antipsychotic, Clozaril, was introduced in 1989. Subsequent atypical antipsychotics include Rispderal, introduced in 1994, and Zyprexa, introduced in 1996. These newer drugs were termed atypicals as they were not associated with many of the side effects of the earlier antipsychotics. While costly, these newer antipsychotics were rapidly adopted by prescribers. From 1995 to 1998 total Medicaid prescriptions for antipsychotics increased 20%, from 9.2 million prescriptions to 11 million prescriptions. Over the same period expenditures increased 160%, from $484 million to $1.3 billion. Atypical antipsychotics accounted for 51% of prescriptions and 89% of spending on antipsychotics in Medicaid in 1998 (the Lewin Group, 2000). In 2002, antipsychotics accounted for $6.4 billion dollars of sales nationally (making them the fourth highest selling class of drugs).[4]

The atypical antipsychotics risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole have become first-line treatment for schizophrenia because they reduce the positive symptoms of psychosis but do not have a high incidence of extrapyramidal symptoms. However, these agents, like other antipsychotics, may take as long as 16 or more weeks to produce a response, and even with prolonged treatment they are unlikely to evoke responses greater than 50% improvement in symptoms. Furthermore, a fraction of patients with psychosis do not respond to any of the antipsychotic monotherapies. This has led to the experimental use of high atypical antipsychotic doses, antipsychotic polypharmacy, and augmentation with other psychotropic drugs, all of which occur commonly in clinical practice.

[4] Erica Goode , "Leading Drugs for Psychosis Come Under New Scrutiny," New York Times May 20, 2003

The use of two antipsychotics simultaneously, sometimes called antipsychotic polypharmacy, is a debatable modern practice in psychiatry. It is based more on experience than evidence. Antipsychotic monotherapies are well accepted treatments of psychosis and their use is supported by large randomized controlled trials and meta-analyses, while the use of two or more antipsychotics has not been repeatedly shown to be safe and effective in large randomized trials.[1] Another issue is the concern of how much of our limited resources should be allocated to polypharmacy. A recent study of polypharmacy within Medi-Cal (the California Medicaid program) showed that 11% of patients who were prescribed antipsychotic medications received two antipsychotics for more than 60 consecutive days and about half of these, approx 5000 patients, received 2 of the first-line agents risperidone, olanzapine or quetiapine, which are among the most expensive drugs covered by the program.[2] Drug costs for polypharmacy patients were three times greater than for patients who received just one drug. Payers such as Medi-Cal are currently looking to reduce the very high overall costs of these drugs by curtailing some high cost-low evidence practices such as atypical antipsychotic polypharmacy rather than complete remove of the availability of some member of the class.[2, 3]

In another study, which evaluated antipsychotic prescribing in a 2003 Medicaid population, the researchers found that, within the subpopulation of Medicaid enrollees who were prescribed antipsychotic medications, 10% had antipsychotic polytherapy and 33% were receiving prescribed dosages outside the range listed in the product labeling.[4] The authors concluded that their findings suggest physicians commonly prescribe antipsychotic medications in a manner that differs from the recommendations described in the prescribing information. The off-label use of atypical antipsychotic medications raises important questions regarding the purpose and applicability of the product labeling and the role and ability of the pharmacist to provide information regarding the risks and benefits of therapy as commonly prescribed.

A leading psychiatrist and clinical researcher suggests that combining antipsychotics should be done only following truly adequate trials of multiple monotherapies, and then with close monitoring in a time-limited trial and continued only when clear therapeutic benefits result.[2]

Application

This indicator will seek to quantify trends in prescribing patterns for antipsychotic medications. The goal of this indicator is to improve quality of care and patient safety, reduce overuse and cost, and reduce drug-drug interactions. The Utah Medicaid Program proposed this indicator. The information on this indicator can be used for public and provider education.

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Indicator 8 – Use of Antibiotics

Antibiotics - Introduction

Antibiotics are drugs given to fight infection. They are effective against bacteria and are the second most commonly prescribed group of medications in the U.S.

Overuse of antibiotics is a major concern as it can lead to antibiotic resistant bacteria. This means that the same antibiotic that is effective against a particular bacterium today may be less effective, or not effective at all, in the future. Other causes of antibiotic resistant bacteria include patients stopping antibiotic treatment prematurely or self-treatment with leftover antibiotics.

This indicator focuses on eight antibiotic classes frequently prescribed on an outpatient basis.

8. Antibiotics

TABLE 8a Use of Antibiotics-Prevalence

Prescription drug classes included in this table are:

- •Natural penicillins/penicillinase-resistant penicillins (including penicillin G and oxacillin) (Class A)
- •Aminopenicillins/extended-spectrum penicillins (including amoxicillin, ampicillin and Augmentin (Class B)
- •Cephalosporins (Class C)
- •Tetracyclines (Class D)
- •Macrolides (including Zithromax, Biaxin and erythromycin) (Class E)
- •Lincosamides (clindamycin) (Class F)
- •Fluoroquinolones (including Cipro and Levaquin) (Class G)
- •Sulfas, trimethoprim and nitrofuran derivatives (including Bactrim and Macrobid) (Class H)

	# of Class A Patients	# of Class B Patients	# of Class C Patients	# of Class D Patients	# of Class E Patients	# of Class F Patients	# of Class G Patients	# of Class H Patients	Total # of Patients on Any Class	# of Patients Per 1,000 Member Years	**Rx PMPY
	663	76,276	25,085	13	20,925	240	51	5,024	94,077	800	
	1,616	34,824	9,369	45	9,247	203	65	2,321	46,913	472	
	6,232	34,166	12,767	9,616	15,296	782	1,526	3,968	65,139	461	
	10,744	46,401	23,539	14,146	25,189	2,350	13,002	16,347	111,493	478	
	4,118	20,170	11,307	5,451	13,194	1,275	9,067	5,810	50,634	492	
	3,524	16,709	10,309	4,817	11,557	1,256	9,853	4,977	44,655	481	
	1,803	9,127	6,460	2,830	6,933	807	7,070	3,259	26,389	508	
	503	2,816	2,946	1,127	2,575	253	3,843	1,976	10,237	528	
	32	296	574	132	324	30	837	446	1,641	597	
	12,278	109,465	43,929	15,525	44,460	2,673	15,720	7,550	193,311	463	
	16,957	131,320	58,427	22,652	60,780	4,523	29,594	36,578	257,867	582	
C AREA											
	22,757	182,364	75,618	29,808	72,216	5,456	33,650	31,926	337,895	639	
	6,478	58,421	26,738	8,369	33,024	1,740	11,664	12,202	113,283	341	
	29,235	240,785	102,356	38,177	105,240	7,196	45,314	44,128	451,178	524	

****Rx PMPY is the average number of prescriptions (for this indicator) per member per year**

Use of Antibiotics - Key Findings

Prevalence:

1) The **overall rate** of patients receiving a medication from one or more of the antibiotic indicator drug classes is **524 patients per 1000 member years.**

2) **This rate is highest** for patients aged 0-4 (800 patients per 1000 member years) and over 85 (597 patients per 1000 member years).

3) **Roughly 60% of patients on antibiotics received some form of penicillin**. Extended-spectrum penicillins like **amoxicillin** and **Augmentin** were most commonly prescribed (89% of all penicillins). Natural penicillins and penicillinase-resistant penicillins like **oxacillin** were less commonly used.

4) **Cephalosporins** and **macrolides** (including erythromycin and Zithromax) were the next most common antibiotic classes prescribed, with between 20-25% of patients on antibiotics receiving each of these classes.

5) The rate of antibiotic use is **higher among women** (582 patients per 1000 member years) than men (463 patients per 1000 member years).

6) The average number of prescriptions per member for 2003 **(RxPMPY)** was **0.74**.

Medication Possession Ratio (MPR)/Persistence:

As opposed to drugs for chronic disease, antibiotics are not medications that patients are typically prescribed for routine use. **As such, Medication Possession Ratio (MPR) and Persistence were not calculated for this indicator.**

Use of Antibiotics - Limitations

1) **Diagnosis information is not available in these records.** This precludes the possibility of examining antibiotic prescribing patterns for various conditions.

Use of Antibiotics - Discussion

Background

After the discovery of penicillin's ability to destroy *Staphylococcus aureus*, several classes of antibiotics have emerged to cure different bacterial infections. This has dramatically increased the life expectancy and reduced mortality related to infectious diseases. Subsequent to the discovery of penicillin in 1940s, 9 classes of antibiotics have emerged in the market: carbapenems, aztreonam, cephalosporins, fluoroquinolones, macrolides, aminoglycosides, ketolides, tetracycline, glycopeptides, and few miscellaneous agents.

Antimicrobial agents are the second most commonly prescribed group of medications in the United States.[1] The Centers for Disease Control and Prevention reported more than 50 million unnecessary antibiotic prescriptions are written annually. The common colds account for 18 million unnecessary prescriptions. Other common contributors are ear infection, bronchitis, sore throat, and sinusitis. Infectious organisms adapt to new environment quickly and over time will become resistant to one or more antibiotics. This process has been exacerbated by inappropriate prescribing and use of antibiotics. Lack of knowledge about natural course of these illnesses contributes to part of the excessive prescribing. Although several wide-spectrum antibiotics have come to market in recent years, physicians often prescribe these therapies when a narrow-spectrum antibiotic would have been sufficient.[2]

Traditionally, physicians have been blamed for these inappropriate prescribing patterns. However, with the development of direct to consumer ads, patients often demand or coerce physicians to prescribe antibiotics for viral infections. In addition, patients contribute to develop resistant organisms by early termination of their therapy or self-treatment with leftover antibiotics for wrong indication. This misuse of antibiotics contributes to development of resistant reinfections or incomplete eradication of the infection. In addition to causing re-infections in individuals, it also

contributes to the spread of antibiotic resistance among community-acquired pathogens, such as *Streptococcus pneumoniae*.

Interventions to improve prescribing patterns have focused on physicians from small-group outreach visits such as academic detailing. Evidence based medicine, guidelines, and expert opinions have been used as reinforcements for selecting the most appropriate treatment. Other studies have focused interventions focusing on the consumers through educating using pamphlets.[3, 4] Despite some success in detailing this message to physicians and educating the public via strategies that target healthcare professionals and patients, there has been an overall increase in antibiotic use.[2] A resolution to this escalating problem resides in the cooperation between physician and patients to combat common infections and differentiate between bacterial versus viral infections.

Description of the Indicator

Antibiotic use (and overuse) is an area of public health concern due to the rise in antibiotic resistant bacteria. Diagnosis data would be helpful for this indicator but pharmacy data alone will provide valuable baseline data. Respiratory diseases and the antibiotics typically used for them would be a focus. Trend data in terms of overall antibiotic use, as well as trends within and between antibiotic classes, would be useful as a marker of increases in appropriate antibiotic usage.

Uses of the Information

HealthInsight proposed this indicator. *HealthInsight* is a partner of the Intermountain Project on Antimicrobial Resistance and Therapy (IMPART) and the Utah Alliance Working for Antibiotic Resistance Education (AWARE). The IMPART and AWARE, a statewide coalition, have explored and used various pharmacy data to (a) monitor antimicrobial resistance among isolates from clinical microbiology laboratories in rural Utah and Idaho, (b) promote appropriate antimicrobial prescribing for acute respiratory tract infections (ARI) in the rural outpatient setting, and (c) track improvements in communities due to interventions. The proposed indicator will

provide statewide information for the AWARE coalition to support their improvement efforts in effective care, reduction of care cost and lessen antibiotic resistant threat for Utahans.

The Utah Alliance Working for Antibiotic Resistance Education (AWARE) Web Site: http://utahaware.com/

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Indicator 9 – Pain Management

Pain Management - Introduction

Symptoms of pain are one of the more frequent reasons people seek medical attention. Causes of pain are many, including acute conditions such as broken bones or surgery and chronic diseases like cancer or arthritis.

Narcotics are the most powerful medications available to treat pain. Balancing adequate control of pain for the patient with the addictive potential of narcotics has been an issue that has received considerable attention both in the medical field and the lay press.

This indicator focuses on use of narcotics for pain management.

9. Pain Management

TABLE 9a. Use of Medications for Control of Pain Management-Prevalence

ription drug classes included in this table are:

A: Combination products, including opioid/non-opioid combinations (APAP, IBU)- dose limited by the non-opioid component:
in, Lorcet (hydrocodone with acetaminophen), Percocet, Tylox (oxycodone with acetaminophen),
ydrocodone with ibuprofen), Tylenol # 2,3,4 (codeine with acetaminophen)

rtial agonists or mixed agonist-antagonists, including dose ceiling effect (lack of additional efficacy after the dose exceeds a predetermined level):
with k antagonist: pentazocine (Talwin), butorphanol (Stadol), nalbuphine (Nubain)
Buprenorphine (injection formulation only)
ose ceiling effect (discontinued use because of unaccept. side effects): codeine (constipation, nausea), meperidine (neurotoxicity, seizure potential) propoxyphene (Darvon)
with functional dose ceiling: tramadol (Ultram)

ull mu agonists, including do not exhibit a ceiling effect with increasing dose: Morphine, hydrocodone, hydromorphone, oxycodone, methadone, oxymorphone, levorphanol,
l

	# of Class A Patients	# of Class B Patients	# of Class C Patients	Total # of Patients on Any Class	# of Patients Per 1,000 Member Years	**Rx PMPY
AGE						
0-4	7,125	107	1,318	8,297	71	0.09
5-9	5,913	95	1,167	6,916	70	0.09
10-17	19,913	475	489	20,311	144	0.23
18-34	69,789	4,239	3,582	71,779	308	0.83
35-44	32,410	3,151	3,429	34,093	331	1.31
45-54	28,685	3,080	3,430	30,621	330	1.37
55-64	16,409	1,927	1,967	17,669	340	1.42
65-84	7,284	1,004	1,411	8,100	418	2.34
85+	1,134	215	497	1,418	516	3.67
GENDER						
Male	75,041	4,781	6,889	79,363	190	0.55
Female	113,621	9,512	10,401	119,841	270	0.92
GEOGRAPHIC AREA						
Urban	144,159	10,387	13,202	152,195	288	0.90
Rural	44,503	3,906	4,088	47,009	142	0.48
TOTAL	188,662	14,293	17,290	199,204	231	0.74

****Rx PMPY is the average number of prescriptions (for this indicator) per member per year**

Pain Management - Key Findings

Prevalence:

1) The **overall rate** of patients receiving a medication from one or more of the pain management indicator drug classes is **231 patients per 1000 member years.**

2) **This rate tends to increase with age**, with a rate for patients aged 65 to 84 of 418 patients per 1000 member years and a rate for patients 85 and older of 516 patients per 1000 member years.

3) While a minority of plan members received a prescription for a medication in this indicator, members could receive more than one prescription over the course of the year. **The average number of prescriptions per member for 2003 (RxPMPY) was 0.74**. Again, this figure was higher for patients ages 65-84 (**2.34**) and 85 and older (**3.67**).

4) A higher proportion of females (270 patients per 1000 member years) than males (190 patients per 1000 member years) received at least one pain management medication.

5) **Combination products** like Lortabs, Vicodin, and Percocet were by far the most common class prescribed, with 95% of patients receiving a drug from this class.

Medication Possession Ratio (MPR)/Persistence:

While many patients will be on medication for chronic pain, not all patients will fit this chronic disease profile. **As such, Medication Possession Ratio (MPR) and Persistence were not calculated for this indicator.**

Pain Management - Limitations

1) **Diagnosis information is not available in these records.** This precludes the possibility of examining prescribing patterns for various conditions.

2) **This indicator focuses specifically on narcotic use.** Medications for pain management other than narcotics (as well as over-the-counter medications) are not included in this indicator.

Pain Management - Discussion

Background

Pain is a common complain presenting to the clinicians office and is an enormous public health problem. Opioids are currently the standard of care for treatment of moderate to severe nociceptive pain. Over the past 10-20 years, several studies were published that documented inadequate pain control in patients with postoperative, cancer and non-malignant chronic pain.[1-7] In response to these reports, professional societies and government and regulatory agencies developed standards and guidelines for the management of acute and chronic pain. Pain is now considered the "fifth vital sign" and hospitals, nursing homes and clinics risk loosing accreditation from the Joint Commission of Accreditation of Healthcare Organizations if they do not assess their patient's pain regularly and respond to it appropriately.

Controlled substances that are prescription drugs, such as opioids, are essential for pain treatment; however they carry risk that extends beyond the usual clinical concern about toxicity. These drugs can become the object of abuse and addiction or be a target for diversion to an illicit market.[8] This potential for abuse, addiction, and diversion raises concern among all clinicians and those in law enforcement, drug regulation, and policy makers.

When potentially abusable drugs are also necessary medicines, assessment and management of drug-related problems can be complex. The parameters of acceptable medical practice include patterns of drug prescription—such as long-term administration of an opioid drug at escalating doses and administration of more than one controlled prescription drug—that may raise a "red flag" for both clinicians and regulators.[8] Problematic drug-related behavior is expressed in many ways and has many causes in the clinical setting. Even relatively severe drug-seeking behaviors in the context of a legitimate medical need, such as uncontrolled pain, cannot immediately be ascribed to abuse or addiction. The desperate search for pain relief, and the complex

psychosocial disturbances accompanying chronic pain, may influence the phenomenology of drug use and greatly complicates the assessment of drug-related problems.[8]

Nevertheless, even patients with severe pain can develop patterns of abuse or addiction, conditions that may lead to criminal activity. Drug abusers may visit multiple physicians and present themselves convincingly so that physicians who are unfamiliar with drug abuse may inadvertently contribute to drug diversion. This method of diversion is called "doctor shopping." Skilled "professional patients" seek out physicians and use them, willingly or unwillingly, as suppliers of drugs that are then diverted to the illicit market.[8] Physicians who encounter such patients must control the behaviors, diagnose the comorbidities, and react in a way that is both medically appropriate and consistent with the laws and regulations that apply to the medical use of controlled drugs. Society has a compelling interest in ensuring both the ready access to controlled prescription drugs when medically needed and ongoing efforts to minimize their abuse and diversion.

Pharmacotherapy

Opioids can be classified in multiple different way; however, for the purpose of this project they have been categorized by their properties (agonist vs partial and mixed agonists) and ingredients (combination products).[9, 10] The full μ-agonists exhibit pain relief at increasing dose without a ceiling effect. The partial agonists or mixed agonist-antagonists may demonstrate a ceiling effect at a predetermined level or a functional limitation where the drug's side effects limit the use of the medication. For example, codeine has high potential for constipation and nausea and meperidene has high potential for neurotoxicity. Finally, there is a group of combination products that is combined with non-opioids. These agents are usually limited by the non-opioid component, which is often acetaminophen or ibuprofen. However, it should be noted Darvocet is an exception where propoxyphene is the limiting component of the combination (Table 1).

Table 1. Opioids drug classification based on dose limiting factor

Class	Limitations	Generic (Brand) Name
Full μ agonists	Do not exhibit a ceiling effect with increasing dose	Morphine, hydrocodone, hydromorphone, oxycodone, methadone, oxymorphone, levorphanol, and fentanyl
	Functional dose ceiling effect (limit use because of unacceptable side effects)	Codeine, meperidine, propoxyphene (Darvon®, Darvocet®)
Partial agonists or mixed agonist-antagonists	Dose ceiling effect (lack of additional efficacy after the dose exceeds a predetermined level)	
	μ agonists with κ antagonist	Pentazocine (Talwin®), Butorphanol (Stadol®), Nalbuphine (Nubain®)
	partial agonist	Buprenorphine (injection formulation only)
	Functional dose ceiling effect (limit use because of unacceptable side effects)	Tramadol (Ultram®)
Combination products	Opioid/non opioid combinations– dose limited by the non-opioid component	1. Hydrocodone with acetaminophen (Lortabs®, Norco®, Vicodin®, Loricet®) 2. Oxycodone with acetaminophen (Percocet®, Tylox®) 3. Hydrocodone with ibuprofen (Vicoprofen®) 4. Codeine with acetaminophen [Tylenol® # (2, 3, 4)]

Application:

The aim of this indicator would be to generate information that can help reduce misuse of opioids and reduce costs associated with expensive opioids therapies. This information will be used to identify variations in treatment modality. The Utah Medicaid Program proposed this indicator because they are concerned about the high prevalence and costs of specific opioids being used in the state of Utah. Other state Medicaid programs have evaluated the prevalence of illicit drug use and prescription misuse among individuals with chronic pain and found high rates of abuse. [11]

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Indicator 10 – Use of Generics

Use of Generics - Introduction

The increasing costs of prescription medications, along with the associated burden to patients and the healthcare system, have been well documented. Generic drugs have the same therapeutic properties as their brand name counterparts. As multiple manufacturers can produce generic drugs (as opposed to brand name drugs still under patent), use of generics can result in significant cost savings.

This indicator examines the ratio of generic vs. brand name (both by prescription and dose) for a selected list of twenty-four medications available in generic form. Aggregate information is also broken out by age group, gender and location (urban/rural).

10. Effective Use of Generic Drugs

TABLE 10a. Use of Generic Drugs (By Specific Drug)

Prescription drugs included in this table are as defined by the 2/12/2003 Utah Medicaid list of non-generic drugs and developed by the University of Utah Pharmacotherapy Outcomes Research Center.

Brand Drug Name Generic Drug Name	BRAND (# of Doses Prscrbd)	GENERIC (# of Doses Prscrbd)	% of Generic Drug Doses	BRAND (# of Prescriptions)	GENERIC (# of Prescriptions)	% of Generic Prescriptions
Aldactone/ spironolactone	6,747	599,723	98.9%	130	13,406	99.0%
Axid/ nizatidine	8,381	114,453	93.2%	194	2,837	93.6%
Betapace/ sotalol	9,658	81,682	89.4%	146	1,366	90.3%
Buspar/ buspirone	21,282	570,417	96.4%	341	11,731	97.2%
Cardizem/ diltiazem	129,134	372,512	74.3%	3,917	13,205	77.1%
Claritin/ loratadine	122,215	38,519	24.0%	2,088	3,343	61.6%
Cylert/ pemoline	6,976	21,246	75.3%	123	504	80.4%
Ditropan/ oxybutynin	188,370	486,991	72.1%	8,956	6,490	42.0%
Eldepryl/ selegiline	300	6,957	95.9%	3	170	98.3%
Glucophage/ metformin	1,639,491	3,555,005	68.4%	21,115	55,828	72.6%
K DUR, Klor-Con/ pot. chloride	123,526	2,747,677	95.7%	2,112	57,604	96.5%
Klonopin/ clonazepam	53,906	2,346,495	97.8%	936	54,044	98.3%
Mycelex/ clotrimazole	43,928	83,101	65.4%	996	4,068	80.3%
Prilosec/ omeprazole	391,816	264,265	40.3%	10,241	15,562	60.3%
Prinivil, Zestril/ lisinopril	120,533	2,347,255	95.1%	2,879	76,224	96.4%
Procardia/ nifedipine	41,542	221,659	84.2%	1,202	7,205	85.7%
Pronestyl/ procainamide	8,024	1,526	16.0%	104	29	21.8%
Prozac, Sarafem/ fluoxetine	442,975	3,689,056	89.3%	15,825	109,035	87.3%
Remeron/ mirtazapine	221,879	110,404	33.2%	9,642	6,238	39.3%
Ritalin/ methylphenidate	927,715	809,404	46.6%	30,598	15,576	33.7%
Soma/ carisoprodol	21,410	1,684,283	98.7%	291	39,188	99.3%
Tranxene/ clorazepate	14,767	221,428	93.7%	189	4,709	96.1%
Ultram/ tramadol	572,994	2,144,732	78.9%	11,723	38,526	76.7%
Vasotec/ enalapril	22,963	617,379	96.4%	544	16,377	96.8%
Total	5,140,877	23,142,826	81.8%	124,314	553,392	81.7%

10. Effective Use of Generic Drugs (cont)

TABLE 10b. Use of Generic Drugs (Aggregate)

	BRAND (# of Doses Prscrbd)	GENERIC (# of Doses Prscrbd)	% of Generic Drug Doses	BRAND (# of Prescriptions)	GENERIC (# of Prescriptions)	% of Generic Prescriptions
AGE						
0-4	37,596	138,337	78.6%	730	3,859	84.1%
5-9	330,763	435,435	56.8%	11,672	8,320	41.6%
10-17	582,333	796,338	57.8%	19,413	20,674	51.6%
18-34	576,238	3,354,274	85.3%	16,086	89,287	84.7%
35-44	709,527	3,996,518	84.9%	16,571	98,552	85.6%
45-54	1,175,900	6,010,548	83.6%	23,852	133,259	84.8%
55-64	1,130,348	5,151,345	82.0%	20,678	110,966	84.3%
65-84	532,154	2,804,357	84.1%	12,579	72,627	85.2%
85+	66,018	455,674	87.3%	2,733	15,848	85.3%
GENDER						
Male	2,356,801	9,077,332	79.4%	55,395	203,350	78.6%
Female	2,784,076	14,065,494	83.5%	68,919	350,042	83.6%
GEOGRAPHIC AREA						
Urban	3,879,452	17,499,596	81.9%	94,096	415,807	81.5%
Rural	1,261,425	5,643,231	81.7%	30,218	137,585	82.0%
TOTAL	5,140,877	23,142,826	81.8%	124,314	553,392	81.7%

Use of Generics - Key Findings

1) Among the generic/brand name drugs studied in this indicator, overall **82% of both prescriptions and doses were for generics**.

2) **The highest volume drugs by prescription were**:

Generic	Brand Name	# of prescriptions	% generic
fluoxetine	Prozac, Sarafem	124860	**87**
lisinopril	Prinivil, Zestril	79103	**96**
metformin	Glucophage	76943	**73**

3) **The highest volume drugs by dose were**:

Generic	Brand Name	# of doses	% generic
metformin	Glucophage	5194496	**68**
fluoxetine	Prozac, Sarafem	4132031	**89**
potassium chloride	K-DUR, Klor-Con	2871203	**96**

4) **By age group, patients aged 5-17 were less likely to receive generics**. While other age groups showed remarkably consistent receipt of generics (between 82% and 86% of prescriptions):

   - For patients aged 5-9, only 41.6% of prescriptions filled were generics
   - For patients aged 10-17, only 51.6% of prescriptions filled were generics

5) Among the twenty-four medications examined in this indicator:

   - Eleven had generic prescriptions filled over 90% of the time
   - Nine had generic prescriptions filled between 50% and 90% of the time
   - Four had generic prescriptions filled less than 50% of the time

Use of Generics - Limitations

1) **This is not an exhaustive list of all generic/brand name drugs available**, but rather a selected list intended to focus on drugs of interest.

2) This analysis is based on 2003 data. This list will need to be updated as generics for other brand name drugs become available. In addition, drugs that become available as over-the counter medications (**such as loratadine (Claritin) in fall 2003**) will need to be watched to see if prescribing volume warrants inclusion in future studies.

Use of Generics - Discussion

Background

The Waxman-Hatch Act or the Drug Price Competition and Patent Term Restoration Act of 1984 permitted abbreviated new drug application process available to drugs approved after 1962. The new legislation protects the brand-name drug patent and did not lower the standards for newer competition, but improves the timeliness of generic products to enter the market. It only requires that a new generic product to demonstrate same bioequivalence of the brand-name product. However, many physicians do not feel bioequivalence and therapeutic effectiveness are necessarily the same, and the acceptance of generic substitution is not universal among healthcare providers and across all therapeutic areas. A nationwide survey on physician beliefs, knowledge, and experience with generic drugs found only 17 percent of physicians could correctly identify the Food and Drug Administration standards for bioequivalency.[1]

The average annual percent increase in prescription drug expenditures between 1990 and 1999 was 12.2%.[2] Generic substitution has been used mainly as a cost-saving measure for patients and third party payers to slow the rate of prescription costs. Physicians prescribe generic prescriptions as their primary means to decrease patient's

prescription economic burden, but they often do not communicate economic savings with their patients because of lack of habit, insufficient time, and concerns over patient discomfort.[3] In the early 1990s, pharmacy benefit managers emerged in the market to contain this increasing trend and many plans provide incentives for pharmacists to promote generic use when patients fill their prescriptions. Pharmacists substitute approximately 83% of brand-name drugs when possible.[4] It has been reported generic substitution is more likely for uninsured prescriptions than prescriptions covered by private third party and indemnity insurance.[4] This is most likely the result of a combination of incentives to the healthcare providers and requests from patients who are sensitive to such cost burden.

The use of generic drugs and the potential accompanying cost savings are the focuses of this indicator. Prescriptions for targeted therapy classes will be tracked and split into brand name and generics. An estimate of potential cost savings can be calculated based on price differential between brand name and generic when generic substitution is possible.

Uses of the Information

The UPDAC health plan representatives proposed this indicator. Potential cost savings that can be had through use of generic drugs are well documented. However, utilization of generic drugs where they are available remains inconsistent and sporadic among patients, providers, and geographic areas.

The percentage of generic drug type prescribed for a number of selected medications will be determined. Learning about trends - at the statewide level, by geographic area, and by patient age - will identify attractive targets for intervention and education by health plans, Utah Medicaid and Children's Health Insurance Programs.

For more information go to FDA Consumer Education Web Page:

What You Should Know About Buying and Using Drug Products

http://www.fda.gov/cder/consumerinfo/DPAdefault.htm

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